Jan.

90332

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Howard Owens Examiner #: _____ Date: 3-31-03

Art Unit: 1623 Phone Number 306-4538 Serial Number: 09/779,447

Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

CM1 8B17 MAILBOX - 8B19

If mor than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search class 1, 4, 6, 8, 10-15, 17 and 18.

* along with the method of inhibiting angiogenesis, please search the associated diseases in claim 15.

* I'm not sure as to whether the compound(s) is/are novel; however the method of use is the patentable invention.

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

****

STAFF USE ONLY

Searcher: _____

Searcher Phone #: 4496

Searcher Location: _____

Date Searcher Picked Up: 4/8/03

Date Completed: 4/8/03

Searcher Prep & Review Time: _____

Clerical Prep Time: 15

Online Time: ~~95~~

Type of Search

NA Sequence (#) _____

AA Sequence (#) _____

Structure (#) 1

Bibliographic _____

Litigation _____

Fulltext _____

Patent Family _____

Other _____

Vendors and cost where applicable

STN ✓

Dialog _____

Questel/Orbit _____

Dr.Link _____

Lexis/Nexis _____

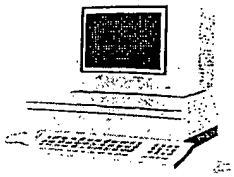
Sequence Systems _____

WWW/Internet _____

Other (specify) _____

PTO-1590 (1-2000)

BioTech-Chem Library
Search Results
Feedback Form (Optional)



Scientific & Technical Information Center

The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact ***the BioTech-Chem searcher*** who conducted the search ***or contact***:

Mary Hale, Supervisor, 308-4258
CM-1 Room 1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* *(Example: 1610)*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Search results were not useful in determining patentability or understanding the invention.

Other Comments:

Drop off completed forms at the **Circulation Desk CM-1**, or send to Mary Hale, **CM1-1E01 or e-mail mary.hale@uspto.gov.**

Jan Delaval
Reference Librarian
Biotechnology & Chemical Libra
CM1 1E07 – 703-308-4498
jan.delaval@usp[illegible].gov

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 14:47:36 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    7 APR 2003  HIGHEST RN 502131-66-0
DICTIONARY FILE UPDATES:   7 APR 2003  HIGHEST RN 502131-66-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L3                STR
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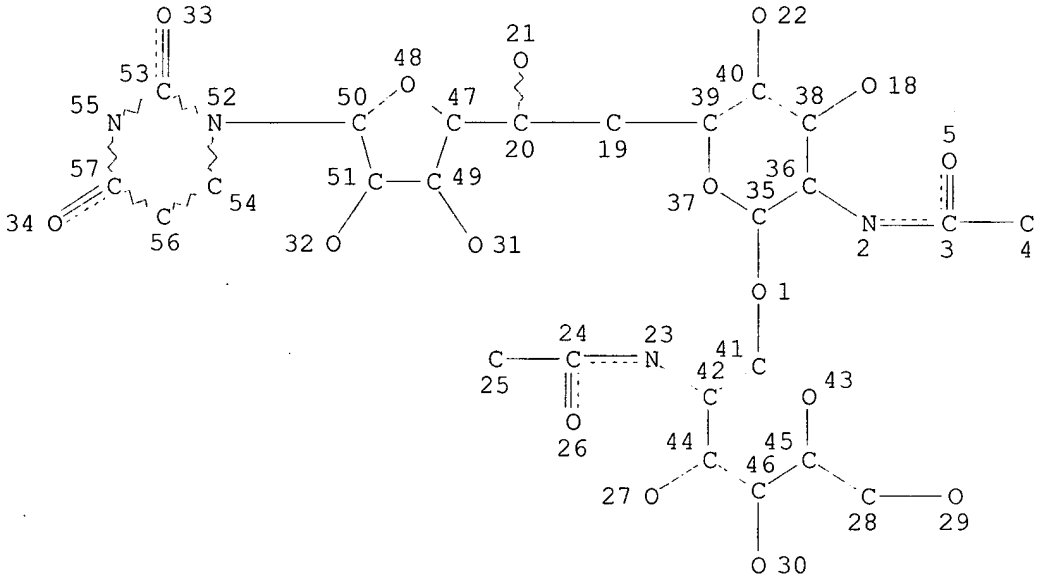


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  45

STEREO ATTRIBUTES: NONE
L5           72 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED    113 ITERATIONS                    72 ANSWERS
SEARCH TIME: 00.00.01
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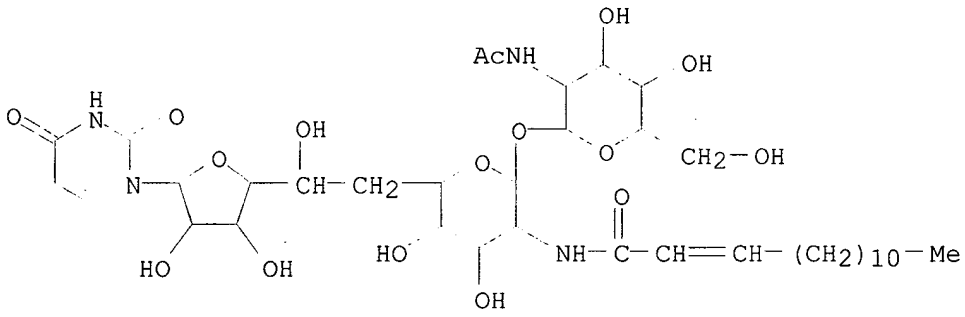
L1 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-45-1 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-1-oxo-2-tetradecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(1-oxo-2-tetradecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN **Tunicamycin A2**
CN Tunicamycin III
DR 82225-27-2
MF C37 H60 N4 O16
LC STN Files: ANABSTR, BEILSTEIN*, CA, CAPLUS, DDFU, DRUGU, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12 REFERENCES IN FILE CA (1962 TO DATE)
12 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:363584

REFERENCE 2: 109:148121

REFERENCE 3: 109:3532

REFERENCE 4: 106:212546

REFERENCE 5: 106:5372

REFERENCE 6: 102:113850

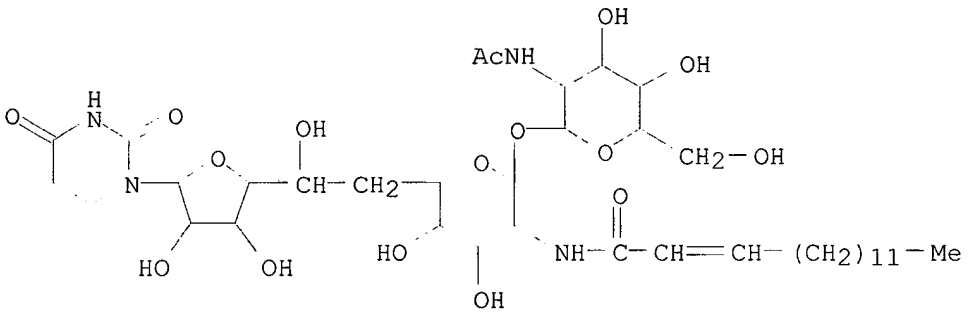
REFERENCE 7: 100:39668

REFERENCE 8: 100:20312

REFERENCE 9: 98:100866

REFERENCE 10: 97:161058

L1 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 73942-09-3 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-1-oxo-2-pentadecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(1-oxo-2-pentadecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN **Tunicamycin B2**
DR 76544-49-5
MF C38 H62 N4 O16
LC STN Files: ANABSTR, BIOSIS, CA, CANCERLIT, CAPLUS, DDFU, DRUGU, MEDLINE, TOXCENTER, USPATFULL



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8 REFERENCES IN FILE CA (1962 TO DATE)
8 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:363584

REFERENCE 2: 109:3532

REFERENCE 3: 103:81384

REFERENCE 4: 100:39668

REFERENCE 5: 100:20312

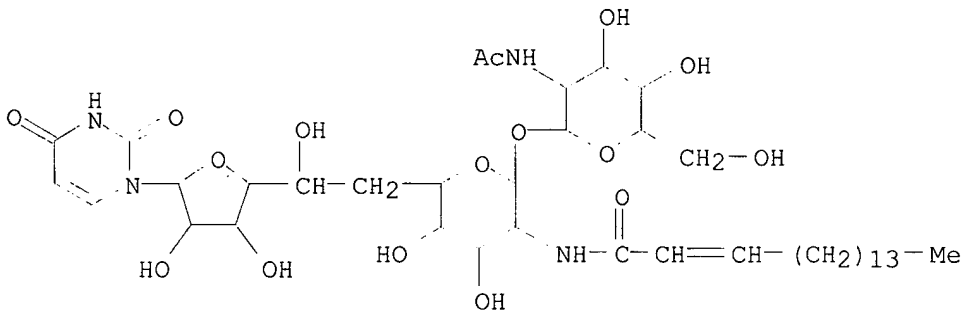
REFERENCE 6: 98:100866

REFERENCE 7: 97:161058

REFERENCE 8: 93:2451

L1 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 73942-08-2 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-1-oxo-2-heptadecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-

.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(1-oxo-2-heptadecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN **Tunicamycin D1**
DR 76544-57-5
MF C40 H66 N4 O16
LC STN Files: ANABSTR, CA, CAPLUS, CSCHEM, MSDS-OHS, NAPRALERT, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

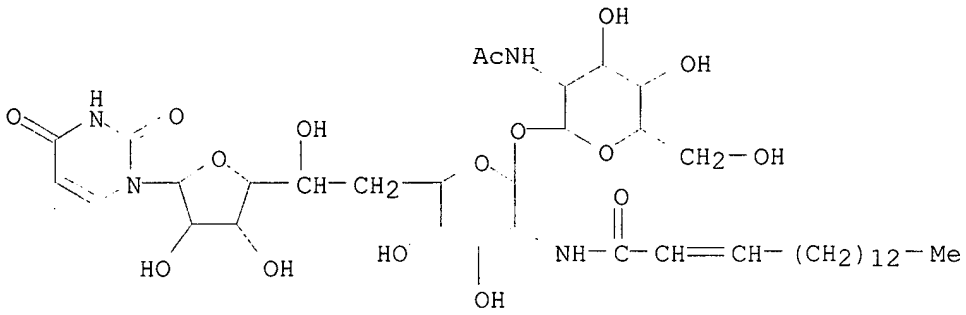
REFERENCE 1: 134:363584

REFERENCE 2: 100:39668

REFERENCE 3: 97:161058

REFERENCE 4: 93:2451

L1 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 73942-07-1 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-1-oxo-2-hexadecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(1-oxo-2-hexadecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN **Tunicamycin C2**
CN Tunicamycin VIII
DR 76544-55-3
MF C39 H64 N4 O16
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CHEMCATS, CSCHEM, MSDS-OHS, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



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REFERENCE 2: 109:148121

REFERENCE 3: 106:5372

REFERENCE 4: 102:113850

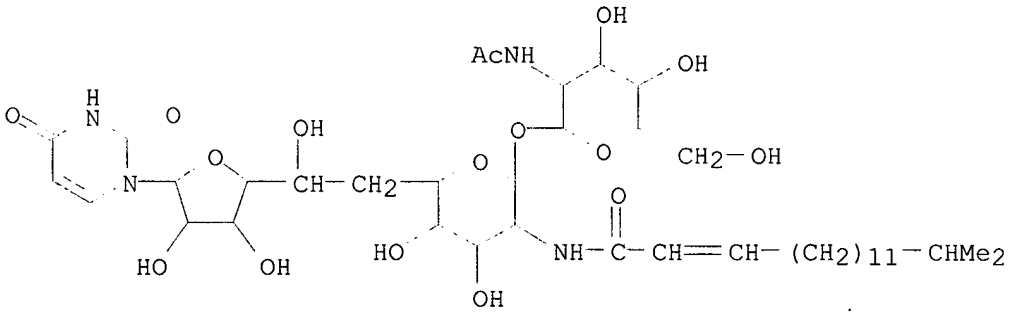
REFERENCE 5: 100:39668

REFERENCE 6: 100:20312

REFERENCE 7: 97:161058

REFERENCE 8: 93:2451

L1 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 66081-38-7 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-15-methyl-1-oxo-2-hexadecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(15-methyl-1-oxo-2-hexadecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN Corynetoxin U 17i
CN Tunicamycin D
CN **Tunicamycin D2**
DR 76544-58-6
MF C40 H66 N4 O16
LC STN Files: ANABSTR, BEILSTEIN*, CA, CAPLUS, CSCHEM, DDFU, DRUGU, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



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8 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:363584

REFERENCE 2: 104:183411

REFERENCE 3: 100:39668

REFERENCE 4: 100:20312

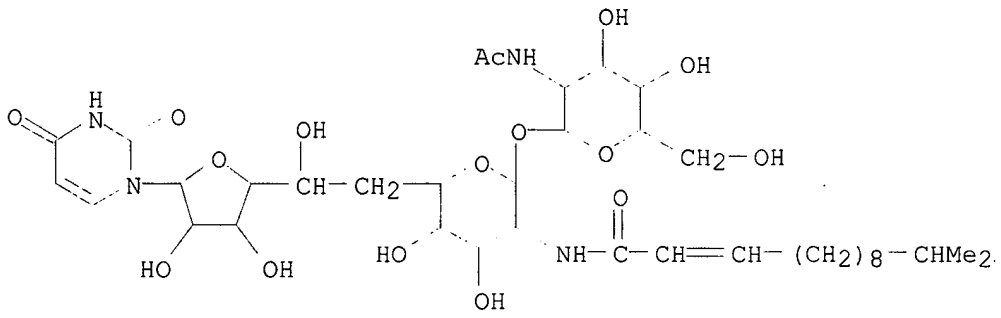
REFERENCE 5: 97:20337

REFERENCE 6: 94:63780

REFERENCE 7: 93:2451

REFERENCE 8: 88:136882

L1 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 66081-37-6 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-12-methyl-1-oxo-2-tridecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(12-methyl-1-oxo-2-tridecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN Streptovirudin C2
CN **Tunicamycin A1**
CN Tunicamycin C
DR 51330-33-7, 76544-44-0, 82264-14-0
MF C37 H60 N4 O16
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, MEDLINE, MSDS-OHS, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



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14 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 6: 100:68635

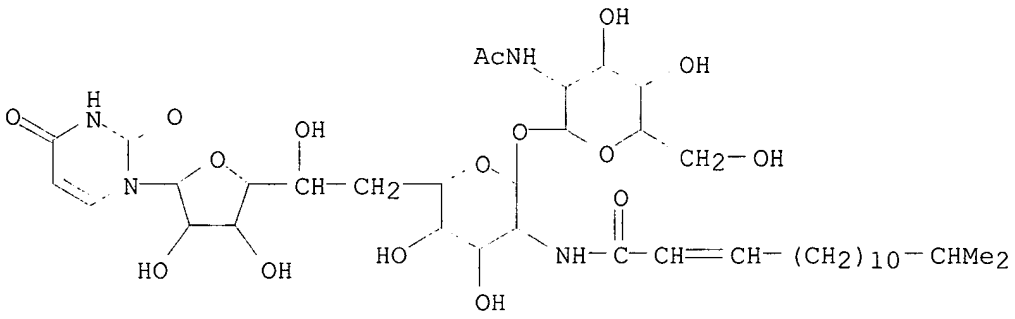
REFERENCE 7: 100:39668

REFERENCE 8: 100:20312

REFERENCE 9: 98:100866

REFERENCE 10: 97:161058

L1 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 66081-36-5 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-14-methyl-1-oxo-2-pentadecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(14-methyl-1-oxo-2-pentadecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN Corynetoxin U 16i
CN Tunicamycin B
CN **Tunicamycin C1**
CN Tunicamycin VII
DR 76544-54-2, 82264-15-1
MF C39 H64 N4 O16
LC STN Files: ANABSTR, BEILSTEIN*, CA, CAPLUS, CSCHEM, DDFU, DRUGU, MSDS-OHS, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1962 TO DATE)
11 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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REFERENCE 2: 109:148121

REFERENCE 3: 109:3532

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REFERENCE 5: 104:6125

REFERENCE 6: 100:39668

REFERENCE 7: 100:20312

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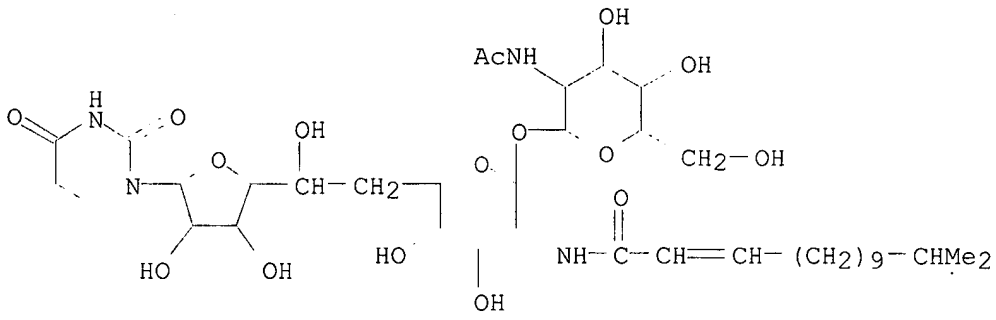
REFERENCE 10: 94:63780

L1 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 66054-36-2 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-13-methyl-1-oxo-2-tetradecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[(13-methyl-1-oxo-2-tetradecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN (+)-Tunicamycin V
CN Tunicamycin A
CN **Tunicamycin B1**
CN Tunicamycin V
DR 76544-48-4
MF C38 H62 N4 O16
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMINFORMRX, DDFU, DRUGU, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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16 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:363584

REFERENCE 2: 130:220286

REFERENCE 3: 125:11326

REFERENCE 4: 122:187184

REFERENCE 5: 121:256211

REFERENCE 6: 118:213430

REFERENCE 7: 109:3532

REFERENCE 8: 106:5372

REFERENCE 9: 105:24559

REFERENCE 10: 102:113850

L1 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 11089-65-9 REGISTRY
CN **Tunicamycin (9CI)** (CA INDEX NAME)
DR 11118-26-6
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, MSDS-OHS, NAPRALERT, RTECS*, TOXCENTER, USPATFULL, VETU
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
661 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
663 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:210387

REFERENCE 2: 138:199509

REFERENCE 3: 138:185209

REFERENCE 4: 138:147380

REFERENCE 5: 138:103336

REFERENCE 6: 138:44521

REFERENCE 7: 138:38077

REFERENCE 8: 138:21926

REFERENCE 9: 138:1005

REFERENCE 10: 137:333152

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L2 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 88263-43-8 REGISTRY
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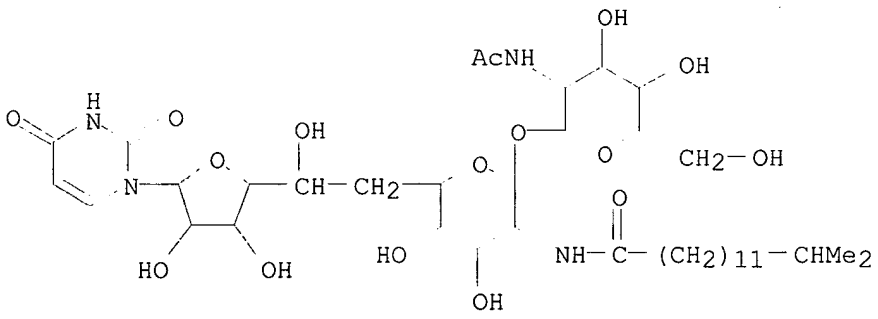
OTHER NAMES:
CN **Tunicamycin VI**
MF C38 H64 N4 O16
LC STN Files: BEILSTEIN*, CA, CAPLUS, NAPRALERT, TOXCENTER
(*File contains numerically searchable property data)



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3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 106:5372

REFERENCE 2: 102:113850

REFERENCE 3: 100:20312

L2 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-56-4 REGISTRY
CN **Tunicamycin C3 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
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REFERENCE 1: 94:71575

L2 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-53-1 REGISTRY
CN **Tunicamycin B6 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 94:71575

L2 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-52-0 REGISTRY
CN **Tunicamycin B5 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 94:71575

L2 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-51-9 REGISTRY
CN **Tunicamycin B4 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 94:71575

L2 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-50-8 REGISTRY
CN **Tunicamycin B3 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CANCERLIT, CAPLUS, DDFU, DRUGU, MEDLINE, TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:363584

REFERENCE 2: 98:241

REFERENCE 3: 94:71575

L2 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2003 ACS

RN 76544-47-3 REGISTRY
CN **Tunicamycin A4 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

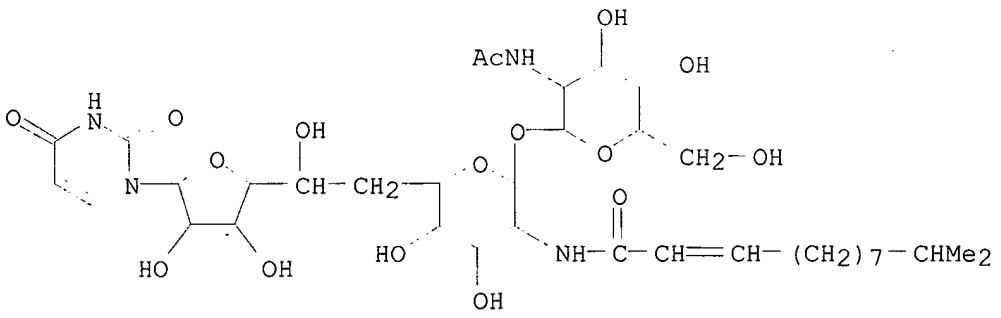
REFERENCE 1: 94:71575

L2 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 76544-46-2 REGISTRY
CN **Tunicamycin A3 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 94:71575

L2 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 73942-10-6 REGISTRY
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideox-10-[[(2E)-11-methyl-1-oxo-2-dodecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,4(1H,3H)-Pyrimidinedione, 1-[[10(E),11S]-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideox-10-[(11-methyl-1-oxo-2-dodecenyl)amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]-
OTHER NAMES:
CN Streptovirudin B2a
CN **Tunicamycin A0**
DR 76544-43-9
MF C36 H58 N4 O16
LC STN Files: ANABSTR, CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:363584

REFERENCE 2: 109:3532

REFERENCE 3: 100:20312

REFERENCE 4: 93:2451

=> d his

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     (FILE 'HOME' ENTERED AT 13:36:32 ON 08 APR 2003)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:36:44 ON 08 APR 2003
               ACT OWENS779/A
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L1             9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (TUNICAMYCIN/CN OR "TUNICAMYC
               ---------
L2             9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (TUNICAMYCIN/CN OR "TUNICAMYC
L3               STR
L4             1 S L3
L5            72 S L3 FUL
               SAV L5 OWENS779B/A
L6               STR L3
L7            63 S L6 CSS FUL SUB=L5
               SAV L7 OWENS779C/A
L8             9 S L5 NOT L1,L2,L7

     FILE 'HCAPLUS' ENTERED AT 13:44:37 ON 08 APR 2003
L9           684 S L1
L10            9 S L2
L11           39 S L7
L12            8 S L8
               E TUNICAMYCIN
L13         3256 S E3-E7
               E TUNICAM
L14           42 S E4-E9
L15           45 S L13,L14(S)(A1 OR A2 OR B1 OR B2 OR C1 OR C2 OR D1 OR D2)
L16         3285 S L9-L15
               E ANGIOGEN/CT
L17        10311 S E4-E9
               E E4+ALL
L18         8360 S E5+NT
               E E10+ALL
L19         3109 S E4+NT
               E E7+ALL
L20         1687 S E3,E4,E2+NT
               E RETINOPATH/CT
               E E4+ALL
L21         2695 S E2
               E DIABET/CT
               E E55+ALL
L22         1568 S E2
               E ATHEROSLCEROTIC PLAQUE/CT
               E ATHEROSCLEROTIC PLAQUE/CT
               E ATHEROSCLERO/CT
               E E4+ALL
L23        24850 S E7-E9,E6+NT
               E E5+ALL
L24        28214 S E5+NT
               E E11+ALL
L25         5727 S E4
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                E SCLERODERM/CT
                E E5+ALL
L26         1615 S E2
                E HYPERTROPH/CT
                E E9+ALL
L27          148 S E2
                E VASCULAR ADHESION/CT
                E ADHESION/CT
                E E19+ALL
L28         7313 S VASCULAR?(L)ADHESION
                E ANGIOFIBROMA/CT
                E E3+ALL
L29           76 S E2
                E TRACHOMA/CT
                E NEOVASCULAR/CT
                E E4+ALL
L30         1809 S E2
L31          187 S E8,E9
                E GLAUCOMA/CT
L32         3130 S E3-E12
                E E4+ALL
L33         3044 S E5,E4+NT
                E E10+ALL
L34         1018 S E3
                E THROMBOSIS/CT
L35         8485 S E3-E21
                E E3+ALL
L36         8562 S E4+NT
                E E12+ALL
L37        17689 S E5,E4+NT
                E E12+ALL
L38        17325 S E7+NT
L39        29065 S E16+NT
L40          839 S E17+NT
L41         1449 S E20+NT OR E24+NT
                E E22+ALL
L42         8562 S E4+NT
                E E17+ALL
L43         2009 S E4
                E RESTENOSIS/CT
                E E3+ALL
L44         2839 S E2,E3
                E OSTEOPOROSIS/CT
L45         8203 S E3-E9
                E E+ALL
                E OSTEOPOROSIS/CT
                E E3+ALL
L46         8204 S E6+NT
                E BONE DENSITY/CT
                E E2+ALL
L47          969 S E2
                E BONE/CT
L48        48248 S E3
L49         5183 S E56,E57
L50         6347 S E186
L51         2261 S E225
L52         6191 S E226
L53         5662 S E249
L54          999 S E250,E251,E252
L55         1007 S E253
                E MACULAR DEGENERATION/CT
                E E3+ALL
L56          738 S E2
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                E ARTHRITIS/CT
L57         12290 S E3-E25
                E E3+ALL
L58         21540 S E6+NT
                E E19+ALL
L59          4641 S E5,E4+NT
                E E7+ALL
                E E20+ALL
L60          1693 S E5,E4+NT
                E E8+ALL
L61         11025 S E10,E11,E9+NT
                E HEMANGIOMAS/CT
                E HEMANGIOMA/CT
                E E3+ALL
L62           363 S E2
                E PSORIASIS/CT
L63          6798 S E3-E5
                E E3+ALL
L64          6798 S E4
                E E4
                E E7+ALL
L65           220 S E2
                E TUMOR/CT
L66           728 S E3
                E E3+ALL
L67         86974 S E2
                E E2+ALL
L68        230289 S E3-E7,E2+NT
                E E105+ALL
L69        155846 S E4,E3+NT
L70        273606 S NEOPLAS?/CW
L71           373 S L16 AND L17-L70
                E BANERJEE D/AU
L72           564 S E3,E7,E46-E48
                E MARTINEZ J/AU
L73           602 S E3-E8
                E MARTINEZ JUAN/AU
L74            30 S E3-E5
L75             5 S L72-L74 AND L16
L76             2 S L75 AND L71
L77             5 S L75,L76
L78            15 S (L1 OR L2 OR L7 OR L8) (L) (THU OR PAC OR PKT)/RL AND L71
L79             5 S L16 AND ?ANGIOGEN?
L80             4 S L79 NOT HYPOXIA
L81             1 S L16 AND ?RETINOPATH?
L82            10 S L16 AND ?DIABET?
L83             0 S L82 AND (EYE OR RETINA OR RETINAL)
L84             0 S L82 AND L81
L85             0 S L78 AND L81,L82
L86             9 S L16 AND (?ATHEROSCLER? OR ?ARTERIOSCLER?)
L87            55 S L16 AND (?SCLERODERM? OR HYPERTROPH? OR SCAR? OR VASCULAR?(L)
L88             0 S L78 AND L87,L86
L89           655 S L16 AND (?NEOPLAS? OR ?TUMOR? OR ?MALIGN? OR ?CANCER? OR ?CAR
L90            14 S L78 AND L89
L91           755 S L78-L90,L71 AND (PD<=20000209 OR PRD<=20000209 OR AD<=2000020
                SEL RN L77

     FILE 'REGISTRY' ENTERED AT 14:22:10 ON 08 APR 2003
L92            11 S E1-E11
L93             1 S L92 AND L1,L2,L5,L7,L8
L94            10 S L92 NOT L93

     FILE 'HCAPLUS' ENTERED AT 14:27:14 ON 08 APR 2003
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                E NUCLEOSIDE/CT
L95         1025 S E34
                E E14+ALL
L96          169 S E51
L97            1 S L95,L96 AND L91

     FILE 'HCAPLUS' ENTERED AT 14:28:55 ON 08 APR 2003
                S GLUCOSAMINE/CN

     FILE 'REGISTRY' ENTERED AT 14:28:55 ON 08 APR 2003
L98            1 S GLUCOSAMINE/CN

     FILE 'HCAPLUS' ENTERED AT 14:28:55 ON 08 APR 2003
L99         5131 S L98
L100       18777 S GLUCOSAMINE
L101          90 S L91 AND L99,L100

     FILE 'REGISTRY' ENTERED AT 14:29:28 ON 08 APR 2003
L102           1 S 7512-17-6

     FILE 'HCAPLUS' ENTERED AT 14:30:02 ON 08 APR 2003
L103        5041 S L102
L104       13257 S ?ACETYLGLUCOSAMINE? OR ACETYL(1W)GLUCOSAMINE
L105          39 S L91 AND L103,L104
L106         116 S L101,L105
L107           3 S L78 AND L106
L108           7 S L77,L107
L109         113 S L91 AND (1 OR 63)/SC,SX
L110          30 S L106 AND L109
L111          13 S L110 AND (LECTIN OR HL OR VIRUS OR STRESS OR NEWCASTLE OR VIT
L112          17 S L110 NOT L111
L113          20 S L108,L112
L114          21 S L91 AND DOLICHOL
L115           3 S L91 AND FACTOR VIII C

     FILE 'REGISTRY' ENTERED AT 14:40:58 ON 08 APR 2003
L116           1 S 11029-02-0
L117           2 S 70431-08-2 OR 113189-02-9
L118           1 S 62213-44-9

     FILE 'HCAPLUS' ENTERED AT 14:43:13 ON 08 APR 2003
L119        2368 S L116 OR L117 OR L118
L120           7 S L119 AND L91
L121          38 S L113-L115,L120 AND L9-L91,L95-L97,L99-L101,L103-L115,L119,L
L122          37 S L121 AND L91
L123          38 S L121,L122
L124          25 S L123 AND (?ANGIOGEN? OR ?DOLICH? OR FACTOR VIII)
L125          13 S L123 NOT L124

     FILE 'REGISTRY' ENTERED AT 14:47:36 ON 08 APR 2003

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:48:11 ON 08 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 8 Apr 2003 VOL 138 ISS 15
FILE LAST UPDATED: 7 Apr 2003 (20030407/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l124 all hitstr tot

L124 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:833506 HCAPLUS
DN 137:333152
TI Methods for inhibiting **angiogenesis**
IN **Banerjee, Dipak K.; Martinez, Juan A.**
PA USA
SO U.S. Pat. Appl. Publ., 48 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-7068
NCL 514050000
CC **1-8** (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002160979	A1	20021031	US 2001-779447	20010209 <--
PRAI US 2000-181312P	P	20000209 <--		

OS MARPAT 137:333152
AB A method for inhibiting **angiogenesis**, including: administering a nucleoside, such as **tunicamycin**, in an amt. effective to inhibit **angiogenesis**, to a patient in need of such treatment. A method for inhibiting **angiogenesis**, including: administering a nucleoside, which comprises **glucosamine**, in an amt. effective to inhibit **angiogenesis**, to a patient in need of such treatment; wherein the nucleoside is administered for a period of time, subsequently the administration of the nucleoside is suspended for a period of time of at least about 1 wk, and subsequently the administration of the nucleoside is resumed.
ST **angiogenesis** inhibitor
IT Glycosylation
(biol.; methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT Cell cycle
(inhibitors; methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT Oligosaccharides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT **Angiogenesis inhibitors**
Human
(methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT **Pyrimidine nucleosides**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)

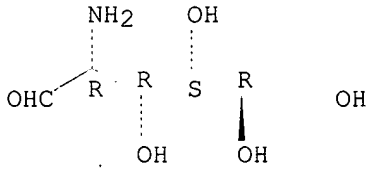
IT **62213-44-9 70431-08-2, Dolichol** phosphate N-**acetylglucosamine**-1-phosphotransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT **113189-02-9**, Blood coagulation **factor VIII**: **C**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT 1402-82-0, Amphomycin **3416-24-8, Glucosamine 7512-17-6D**, N-**Acetylglucosamine**, derivs. **11089-65-9, Tunicamycin**
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses) (methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
IT **62213-44-9 70431-08-2, Dolichol** phosphate N-**acetylglucosamine**-1-phosphotransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
RN 62213-44-9 HCAPLUS
CN Mannosyltransferase, guanosine diphosphomannose-dolichol phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 70431-08-2 HCAPLUS
CN Acetylglucosamine-1-phosphotransferase, uridine diphosphoacetylglucosamine-dolichyl phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **113189-02-9**, Blood coagulation **factor VIII**: **C**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
RN 113189-02-9 HCAPLUS
CN Blood-coagulation factor VIII, procoagulant (9CI) (CA INDEX NAME)

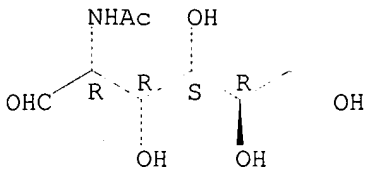
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **3416-24-8, Glucosamine 7512-17-6D**, N-**Acetylglucosamine**, derivs. **11089-65-9, Tunicamycin**
RL: **PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses) (methods for inhibiting **angiogenesis** with nucleosides such as **tunicamycin** and related substances)
RN 3416-24-8 HCAPLUS
CN D-Glucose, 2-amino-2-deoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 7512-17-6 HCAPLUS
CN D-Glucose, 2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:754862 HCAPLUS
DN 134:260978
TI **Tunicamycin** inhibits capillary endothelial **cell proliferation** by inducing apoptosis. Targeting the **dolichol** pathway for generation of new **antiangiogenic** therapeutics
AU **Martinez, Juan A.**; Torres-Negron, Ivette; Amigo, Lilla A.; Roldan, Rossely A.; Mendez, Alba; **Banerjee, Dipak K.**
CS Department of Biochemistry, School of Medicine, University of Puerto Rico, San Juan, 00936-5067, P. R.
SO Advances in Experimental Medicine and Biology (**2000**), 476(Angiogenesis: From the Molecular to Integrative Pharmacology), 197-208
CODEN: AEMBAP; ISSN: 0065-2598
PB Kluwer Academic/Plenum Publishers
DT Journal
LA English
CC **1-6** (Pharmacology)
AB The bovine adrenal medulla microvascular endothelial cells used in this study undergo cellular proliferation and differentiation upon culturing in vitro, as obsd. both by light and SEM. The cells also respond to the growth-promoting activity of serum and basic fibroblast growth factor (FGF2). Flow-cytometric anal. of a synchronized culture established that cells take 68 h to complete one cell cycle, spending 36 h in the G1 phase, 8 h in the S phase, and 24 h in the G2 + M phase when cultured in medium contg. 2% heat-inactivated fetal bovine serum. At 10% serum, or in the presence of FGF2 (10-100 ng/mL), the length of the cell cycle is reduced to 56 h due to shortening of the G1 phase by 12 h. **Tunicamycin** (a **glucosamine**-contg. pyrimidine nucleotide and an inhibitor of glucosaminyl-1-phosphate [GlcNAc 1-P] transferase, the first step of Glc3Man9GlcNAc2-PP-Dol biosynthesis) inhibits endothelial **cell proliferation** by inducing apoptosis, as obsd. by flow cytometry and DNA laddering. Cell shrinkage, compaction of nuclei, membrane fragmentation, etc., all typical of the apoptotic response, are frequently seen by light microscopy in the presence of **tunicamycin**. SEM also showed a considerable amt. of cell surface blebbing. Accumulation of an immunopos. cell-specific asparagine-linked (N-linked) glycoprotein, **Factor VIII:C**, in the absence of Glc3Man9GlcNAc2-PP-Dol in **tunicamycin**-treated cells has been proposed as an apoptotic triggering mechanism under these exptl. conditions.
ST **tunicamycin angiogenesis** inhibitor capillary **cell proliferation** apoptosis
IT Capillary vessel
(endothelium; **tunicamycin** inhibition of capillary endothelial **cell proliferation** by inducing apoptosis)
IT Apoptosis

Cell proliferation
(**tunicamycin** inhibition of capillary endothelial **cell proliferation** by inducing apoptosis)
IT **11089-65-9, Tunicamycin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**tunicamycin** inhibition of capillary endothelial **cell proliferation** by inducing apoptosis)
IT **11029-02-0, Dolichol**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tunicamycin** inhibition of capillary endothelial **cell proliferation** by inducing apoptosis and targeting the **dolichol** pathway)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Banerjee, D; Acta Biochimica Polonica 1994, V41, P275 HCAPLUS
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(29) Zimmerman, J; Yeast 1996, V12, P765 HCAPLUS
IT **11089-65-9, Tunicamycin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**tunicamycin** inhibition of capillary endothelial **cell proliferation** by inducing apoptosis)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **11029-02-0, Dolichol**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**tunicamycin** inhibition of capillary endothelial **cell proliferation** by inducing apoptosis and targeting the **dolichol** pathway)
RN 11029-02-0 HCAPLUS
CN Dolichol (7CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:676022 HCAPLUS
DN 132:10759
TI Overexpression of a gene that encodes the first enzyme in the biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin** and obviates the **tunicamycin**-induced unfolded protein response
AU Koizumi, Nozomu; Ujino, Tokuko; Sano, Hiroshi; Chrispeels, Maarten J.
CS Nara Institute of Science and Technology, Nara, 630-0101, Japan
SO Plant Physiology (**1999**), 121(2), 353-361
CODEN: PLPHAY; ISSN: 0032-0889
PB American Society of Plant Physiologists
DT Journal
LA English
CC 11-1 (Plant Biochemistry)
Section cross-reference(s): 3
AB The **cytotoxic** drug **tunicamycin** kills cells because it is a specific inhibitor of UDP-N-**acetylglucosamine**: **dolichol** phosphate N-**acetylglucosamine**-1-P transferase (GPT), an enzyme that catalyzes the initial step of the biosynthesis of **dolichol**-linked oligosaccharides. In the presence of **tunicamycin**, asparagine-linked glycoproteins made in the endoplasmic reticulum are not glycosylated with N-linked glycans, and therefore may not fold correctly. Such proteins may be targeted for breakdown. Cells that are treated with **tunicamycin** normally experience an unfolded protein response and induce genes that encode endoplasmic reticulum chaperones such as the binding protein (BiP). We isolated a cDNA clone for Arabidopsis GPT and overexpressed it in Arabidopsis. The transgenic plants have a 10-fold higher level of GPT activity and are resistant to 1 .mu.g/mL **tunicamycin**, a concn. that kills control plants. Transgenic plants grown in the presence of **tunicamycin** have N-glycosylated proteins and the drug does not induce BiP mRNA levels as it does in control plants. BiP mRNA levels are highly induced in both control and GPT-expressing plants by azetidine-2-carboxylate. These observations suggest that excess GPT activity obviates the normal unfolded protein response that cells experience when exposed to **tunicamycin**.
ST Arabidopsis **dolichol** phosphate **acetylglucosamine** phosphotransferase gene sequence
IT Glycopeptides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(asparagine-contg.; overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**)
IT Gene, plant
RL: PRP (Properties)
(for UDP-N-**acetylglucosamine**:**dolichol** phosphate N-**acetylglucosamine**-1-P transferase; overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**)
IT Arabidopsis thaliana
DNA sequences
Protein sequences
cDNA sequences
(overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**)
IT 251358-61-9
RL: PRP (Properties)
(amino acid sequence; overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to

tunicamycin)
IT 237054-66-9, GenBank D88036 237054-67-0, GenBank D88037
RL: PRP (Properties)
(nucleotide sequence; overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**)
IT **11089-65-9, Tunicamycin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**
)
IT **70431-08-2**
RL: PRP (Properties)
(overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**
)
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IT **11089-65-9, Tunicamycin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**
)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **70431-08-2**
RL: PRP (Properties)
(overexpression of gene that encodes first enzyme in biosynthesis of asparagine-linked glycans makes plants resistant to **tunicamycin**
)
RN 70431-08-2 HCAPLUS
CN Acetylglucosamine-1-phosphotransferase, uridine diphosphoacetylglucosamine-dolichyl phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:205770 HCAPLUS
DN 130:350283
TI Regulation of UDP-N-**acetylglucosamine:dolichyl**-phosphate N-**acetylglucosamine**-1-phosphate transferase by retinoic acid in P19 cells
AU Meissner, Joachim D.; Naumann, Andreas; Mueller, Walter H.; Scheibe, Renate J.
CS Zentrum Physiologie, Medizinische Hochschule Hannover, Hannover, 30623, Germany
SO Biochemical Journal (**1999**), 338(2), 561-568
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
AB **Dolichyl** phosphate N-**acetylglucosamine**-1-phosphotransferase (I) is the 1st enzyme in the **dolichol** pathway of protein N-glycosylation, and is implicated in the developmental programs of a variety of eukaryotes. In the present study, the authors describe the effects of all-trans-retinoic acid (RA) on the levels of I protein and enzymic activity, and on the transcription rate of the I gene, in mouse P19 **teratocarcinoma** cells. RA caused a dose-dependent and protein synthesis-dependent induction of enzyme activity. The max. induction of I activity (.apprx.3-fold) required 2 days of exposure to 1 .mu.M RA. Induced I activity also resulted in an increase in the rate of incorporation of [3H]mannose into Glc3Man9GlcNAc2. Enzymic activities paralleled I gene expression. The I gene was induced (2-fold) after 7 h of RA treatment. An .apprx.3-fold increase in a 48-kDa I protein and .apprx.4-fold increases in the levels of 3 I transcripts (1.8, 2.0 and 2.2 kb) were obsd. after 2 days of RA treatment. The enhanced levels of I protein and mRNAs began to decline 3 days after the initiation of differentiation, and I expression was down-regulated during cellular differentiation. I activity decreased .apprx.2.8-fold to a const. level in differentiated P19 cells. The results indicated that the RA-induced enzyme activity was mainly detd. by increased transcription of the I gene. RA-treated P19 cells were .apprx.4-fold more resistant to **tunicamycin**, a fungal antibiotic which inhibits I, than were control cells. In addn., I activity in membranes from RA-treated P19

cells exhibited .apprx.4-fold increased resistance to **tunicamycin** compared with activity in membranes from untreated control cells, demonstrating that resistance to **tunicamycin** was correlated with induced I activity. Furthermore, increased I activity had regulatory significance with regard to the rate of incorporation of [3H]mannose into Glc3Man9GlcNAc2-P-P-**dolichol** and into glycoproteins. Together, the data provide addnl. insights into the hormonal regulation of I and present evidence that the RA-mediated induction of I has a regulatory impact on the **dolichol** pathway.

ST **dolichyl** phosphate **acetylglucosaminephosphotransferase** induction retinoate P19 cell differentiation

IT Animal cell line
(P19; induction of **dolichyl** phosphate N-**acetylglucosamine**-1-phosphotransferase by retinoic acid in P19 cells)

IT mRNA
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(for **dolichyl** phosphate **acetylglucosaminephosphotransfer ase**; induction of **dolichyl** phosphate N-**acetylglucosamine**-1-phosphotransferase by retinoic acid in P19 cells)

IT Cell differentiation
(induction of **dolichyl** phosphate N-**acetylglucosamine** -1-phosphotransferase by retinoic acid in P19 cells)

IT 302-79-4, all-trans-Retinoic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(induction of **dolichyl** phosphate N-**acetylglucosamine** -1-phosphotransferase by retinoic acid in P19 cells)

IT **70431-08-2P, Dolichyl** phosphate N-**acetylglucosamine**-1-phosphotransferase
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(induction of **dolichyl** phosphate N-**acetylglucosamine** -1-phosphotransferase by retinoic acid in P19 cells)

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IT **70431-08-2P, Dolichyl** phosphate N-**acetylglucosamine**-1-phosphotransferase
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(induction of **dolichyl** phosphate N-**acetylglucosamine**-1-phosphotransferase by retinoic acid in P19 cells)

RN 70431-08-2 HCAPLUS

CN Acetylglucosamine-1-phosphotransferase, uridine diphosphoacetylglucosamine-dolichyl phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:204255 HCAPLUS

DN 130:350617

TI Expression of Glc3Man9GlcNAc2-PP-Dol is a prerequisite for capillary endothelial **cell proliferation**

AU **Martinez, Juan A.**; Torres-Negron, Ivette; Amigo, Lilia A.; **Banerjee, Dipak K.**

CS Department of Biochemistry, School of Medicine, University of Puerto Rico, San Juan, 00936-5067, P. R.

SO Cellular and Molecular Biology (Paris) (**1999**), 45(1), 137-152
CODEN: CMOBEF; ISSN: 0145-5680

PB C.M.B. Association

DT Journal

LA English

CC 14-5 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13

AB Protein N-glycosylation has been proposed to be intimately involved in the migration, proliferation and differentiation of endothelial cells. Using a synchronized, non-transformed capillary endothelial cell line from bovine adrenal medulla as a model, and the N-glycosylation inhibitor, **tunicamycin**, the authors elucidated the mol. basis of the

dolichol pathway in the **angiogenic** process. The synchronized culture required .apprx.68 h to complete 1 cell cycle, cells spending nearly 36 h in the G1 phase, 8 h in the S phase, and 24 h in the G2 + M phase when maintained in 2% fetal bovine serum (heat-inactivated). The cell cycle however, was shortened due to a redn. of the G1 phase by 12-16 h when the serum concn. was increased to 10%, or when .beta.-fibroblast growth factor (1 or 10 ng) was added into the culture media contg. 2% serum. Light microscopy and SEM both supported these proliferative responses. Serum concn. below 2% arrested **cell proliferation** and induced capillary lumen-like structure formation with 48 h. Expression of blood clotting antigen **factor VIII:C** (a 270-kDa N-linked glycoprotein and a marker of these endothelial cells) preceded the endothelial **cell proliferation** and established a temporal relation. **Tunicamycin**, an inhibitor of Glc3Man9GlcNAc2-PP-Dol (oligosaccharide-lipid; OSL) biosynthesis, a prerequisite for N-linked protein glycosylation in the endoplasmic reticulum, inhibited cell growth and proliferation in a time- and dose-dependent manner with a concomitant accumulation of immunopos., nonglycosylated **factor VIII :C** in the conditioned media. **Tunicamycin** also caused surface blebbing and induction of programmed cell death (PCD; apoptosis) within 32 h. Absence of cellular growth and proliferation, surface blebbing and the induction of PCD in the presence of **tunicamycin** , provided conclusive evidence that normal expression of OSL is an essential event for capillary proliferation during **angiogenesis**.

ST capillary endothelial **cell proliferation** oligosaccharide lipid expression **angiogenesis**

IT Capillary vessel
Capillary vessel
(endothelium; expression of Glc3Man9GlcNAc2-PP-Dol is a prerequisite for capillary endothelial **cell proliferation** in **angiogenesis**)

IT **Angiogenesis**
Cell proliferation
(expression of Glc3Man9GlcNAc2-PP-Dol is a prerequisite for capillary endothelial **cell proliferation** in **angiogenesis**)

IT 68444-48-4
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(expression of Glc3Man9GlcNAc2-PP-Dol is a prerequisite for capillary endothelial **cell proliferation** in **angiogenesis**)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L124 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:955311 HCAPLUS
DN 124:51690
TI **Dolichyl** phosphate, a potent inducer of apoptosis in rat **glioma** C6 cells
AU Yasugi, Etsuko; Yokoyama, Yoshiko; Seyama, Yousuke; Kano, Kazutaka; Hayashi, Yokichi; Oshima, Mieko
CS Division of Biochemistry and Nutrition, International Medical Center of Japan, Toyama, 162, Japan
SO Biochemical and Biophysical Research Communications (**1995**), 216(3), 848-53
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
AB Exposure of rat **glioma** C6 cells to **dolichyl** phosphate resulted in cell shrinkage followed by nuclear fragmentation and internucleosomal cleavage of genomic DNA, yielding ladder patterns of oligonucleosomal fragments, all characteristics of apoptosis. This phenomenon occurred in a dose- and time-dependent manner. **Dolichol** and prenol failed to induce apoptosis. Inhibitors of N-glycosylation, **tunicamycin** and swainsonine, had no apparent effect on **dolichyl** phosphate-induced apoptosis. Apoptotic changes were also obsd. in HL-60 cells, SIRC cells and HeLa cells. Thus, **dolichyl** phosphate functions as a potential apoptosis inducer as well as an essential carrier lipid in the biosynthesis of N-linked glycoprotein.
ST **dolichyl** phosphate apoptosis **glioma** cell
IT Apoptosis
(**dolichyl** phosphate as potent inducer of apoptosis in rat **glioma** C6 cells)
IT **HeLa cell**
(**dolichyl** phosphate as potent inducer of apoptosis in rat **glioma** C6 cells and other cells)
IT Animal cell line
(C-6, **dolichyl** phosphate as potent inducer of apoptosis in rat **glioma** C6 cells)
IT Animal cell line
(HL-60, **dolichyl** phosphate as potent inducer of apoptosis in rat **glioma** C6 cells and other cells)

IT Animal cell line
(SIRC, **dolichyl** phosphate as potent inducer of apoptosis in rat **glioma** C6 cells and other cells)
IT 12698-55-4, **Dolichyl** phosphate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**dolichyl** phosphate as potent inducer of apoptosis in rat **glioma** C6 cells)

L124 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:292981 HCAPLUS
DN 122:47487
TI Mevalonate dependency of the early cell cycle mitogenic response to epidermal growth factor and prostaglandin F2.alpha. in Swiss mouse 3T3 cells
AU Ortiz, Marcela B.; Goin, Mercedes; Gomez de Alzaga, Maria B.; Hammarstrom, Swen; Jimenez de Asua, Luis
CS Inst. Investigaciones, Ingenieria Genet. Biol. Mol., Buenos Aires, 1428, Argent.
SO Journal of Cellular Physiology (**1995**), 162(1), 139-46
CODEN: JCLLAX; ISSN: 0021-9541
PB Wiley-Liss
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB Lovastatin (LOV), a hydroxy-methylglutaryl-CoA (HMGCoA) reductase competitive inhibitor, blocks epidermal growth factor (EGF)- or prostaglandin F2.alpha. (PGF2.alpha.)-induced mitogenesis in confluent resting Swiss 3T3 cells. This inhibition occurs even in the presence of insulin, which potentiates the action of these mitogens in such cells. LOV exerts its effect in a 2-80 .mu.M concn. range, with both mitogens attaining 50% inhibition at 7.5 .mu.M. LOV exerted its effect within 0-8 h following mitogenic induction. Mevanolactone (10-80 .mu.M) in the presence of LOV could reverse LOV inhibition within a similar time period. LOV-induced blockage of PGF2.alpha. response is reflected in a decrease in the rate of cell entry into S phase. Neither cholesterol, ubiquinone, nor **dolichols** of various lengths could revert LOV blockage. In EGF- or PGF2.alpha.-stimulated cells, LOV did not inhibit [3H]leucine or [3H]mannose incorporation into proteins, while **tunicamycin**, an inhibitor of N' glycosylation, prevented this last phenomenon. Thus, it appears that LOV exerts its action neither by inhibiting unspecific protein synthesis nor by impairing the N' glycosylation process. These findings strongly suggest that either EGF or PGF2.alpha. stimulations generate early cell cycle signals which induce mevalonate formation, N'glycoprotein synthesis, and proliferation. The causal relation of these events to various mechanisms controlling the onset of DNA synthesis is also discussed.
ST mevalonate EGF PGF2 signaling mitogen
IT Glycosidation
(N-glycoproteins and mevalonate involvement in EGF and PGF2.alpha. signaling mechanisms in early cell cycle mitogenic responses in 3T3 cells)
IT Cell cycle
Cell division
Cell proliferation
Deoxyribonucleic acid formation
Signal transduction, biological
Translation, genetic
(mevalonate involvement in EGF and PGF2.alpha. signaling mechanisms in early cell cycle mitogenic responses in 3T3 cells)
IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); PROC (Process)
(N-linked, N-glycoproteins and mevalonate involvement in EGF and PGF2.alpha. signaling mechanisms in early cell cycle mitogenic responses in 3T3 cells)
IT Interphase, biological
(S-phase, mevalonate involvement in EGF and PGF2.alpha. signaling mechanisms in early cell cycle mitogenic responses in 3T3 cells)
IT 150-97-0, Mevalonic acid
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mevalonate involvement in EGF and PGF2.alpha. signaling mechanisms in early cell cycle mitogenic responses in 3T3 cells)
IT 551-11-1, PGF2.alpha. 62229-50-9, Epidermal growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mevalonate involvement in EGF and PGF2.alpha. signaling mechanisms in early cell cycle mitogenic responses in 3T3 cells)

L124 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:295182 HCAPLUS
DN 120:295182
TI Is asparagine-linked protein glycosylation an obligatory requirement for **angiogenesis**?
AU **Banerjee, Dipak K.**; Vendrell-Ramos
CS Sch. Med., Univ. Puerto Rico, San Juan, 00936-5067, P. R.
SO Indian Journal of Biochemistry & Biophysics (**1993**), 30(6), 389-94
CODEN: IJBBBQ; ISSN: 0301-1208
DT Journal
LA English
CC 13-6 (Mammalian Biochemistry)
AB Dependence of protein N-glycosylation on capillary endothelial **cell proliferation** has been studied. Amphomycin, a potent N-glycosylation inhibitor, inhibited capillary endothelial **cell proliferation** in a dose-dependent manner. .beta.-Agonist isoproterenol as well as other intracellular cAMP enhancing agents, viz. cholera toxin, prostaglandin E1 and 8Br-cAMP, also enhanced capillary endothelial **cell proliferation**. In addn. to **cell proliferation**, isoproterenol also enhanced protein glycosylation in these cells. Isoproterenol effect was mediated by .beta.-adrenoreceptors, as it got reduced on pre-treatment of cells with either atenolol or ICI 118, 551 or propranolol. Furthermore, isoproterenol stimulation of protein glycosylation by exogenous **dolichyl** monophosphate and its inhibition by **tunicamycin** (GlcNAc-1P transferase inhibitor) supported the concept that isoproterenol specifically stimulated protein N-glycosylation event(s) in the cell.
ST glycoprotein glycosylation **angiogenesis**; endothelium proliferation N linked glycoprotein
IT Blood vessel
(formation of, asparagine-linked glycoprotein glycosylation role in)
IT **Cell proliferation**
(of vascular endothelium, asparagine-linked glycoprotein glycosylation role in)
IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(N-linked, endothelium proliferation requirement for, **angiogenesis** in relation to)
IT Capillary vessel
(endothelium, proliferation of, asparagine-linked glycoprotein glycosylation role in)
IT 60-92-4, CAMP
RL: BIOL (Biological study)

(asparagine-linked glycoprotein glycosylation and **cell proliferation** regulation by, in vascular endothelium)

L124 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:469309 HCAPLUS
DN 119:69309
TI Isoprenoid regulation of cell growth: Identification of mevalonate-labeled compounds inducing DNA synthesis in human breast **cancer** cells depleted of serum and mevalonate
AU Wejde, Johan; Carlberg, Magdalena; Hjertman, Magnus; Larsson, Olle
CS Karolinska Inst., Karolinska Hosp., Stockholm, S-104 01, Swed.
SO Journal of Cellular Physiology (**1993**), 155(3), 539-48
CODEN: JCLLAX; ISSN: 0021-9541
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB Growth arrest induced by serum depletion and/or treatment with mevinolin (an inhibitor of mevalonate synthesis) in the human breast **cancer** cell line Hs578T was overcome by exogenous mevalonate, indicating that some product or metabolite of mevalonate may be involved in the mediation of serum-regulated growth of these cells. In the search for such compds. the authors first tested a variety of known end products of mevalonate with respect to their ability to counteract the inhibition of DNA synthesis caused by serum-free medium and mevinolin. High doses (10 .mu.g/mL) of **dolichol**-20 caused a partial counteraction. After straight-phase HPLC purifn. of endogenous lipids, isolated from 3H- or 14C-mevalonate-labeled Hs578T cultures, the authors found that non-sterol lipids co-eluting with **dolichols** efficiently induced DNA synthesis. After further purifn. with reverse-phase HPLC it was confirmed that virtually all of this effect was achieved by compd.(s) (seen as a single UV and radioactive peak) co-eluting with **dolichol**-20. Nanogram doses, at most, of this (these) compd.(s) elicited a substantial stimulation of DNA synthesis. The lipid(s) also counteracted the inhibition by mevinolin of N-linked glycosylation, indicating that it (they) also interfere(s) with this processing. Since treatment with **tunicamycin** (an inhibitor of N-linked glycosylation) abolished this growth-stimulative effect, N-linked glycosylation seems to be a necessary event in the processes leading to lipid-induced initiation of DNA synthesis.
ST DNA formation breast **carcinoma** isoprenoid; Hs578T **cell proliferation** lipid
IT Isoprenoids
Lipids, biological studies
RL: BIOL (Biological study)
(DNA formation in human mammary **carcinoma** stimulation by)
IT Glycosidation
(DNA formation in human mammary **carcinoma** stimulation by isoprenoids in relation to)
IT **Cell proliferation**
Deoxyribonucleic acid formation
(in mammary **carcinoma**, of human, isoprenoid stimulation of)
IT Animal cell line
(Hs-578T, DNA formation in, of human, isoprenoid stimulation of)
IT Mammary gland
(**neoplasm, carcinoma**, DNA formation in, of human, isoprenoid stimulation of)
IT 2067-66-5, **Dolichol**-20
RL: BIOL (Biological study)
(DNA formation in human mammary **carcinoma** stimulation by)

L124 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1989:400365 HCAPLUS
DN 111:365

TI The role of N-linked glycosylation in the regulation of activity of 3-hydroxy-3-methylglutaryl-coenzyme A reductase and proliferation of SV-40-transformed 3T3 cells
AU Larsson, Olle; Engstroem, Wilhelm
CS Dep. Tumour Pathol., Karolinska Hosp., Stockholm, S-104 01, Swed.
SO Biochemical Journal (**1989**), 260(2), 597-600
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
CC **1-6** (Pharmacology)
Section cross-reference(s): 14
AB The effects of glycosylation inhibitors on the proliferation of SV40-transformed 3T3 cells were examd. in vitro. Whereas swainsonine and castanospermine, which inhibit distal steps in the glycosylational processing, exerted marginal or no effects on **cell proliferation**, a proximal inhibitor, **tunicamycin**, efficiently decreased the rate of DNA synthesis and also inhibited the activity of 3-hydroxy-3-methyglutaryl-CoA (HMG-CoA) reductase. The inhibitory effects of **tunicamycin** on **cell proliferation** could be partially reversed by addn. of **dolichol**, a metabolite in the pathway regulated by HMG-CoA reductase. This finding suggests that **tunicamycin** exerts .gtoreq.1 of its effects on **cell proliferation** by modulating the activity of HMG-CoA reductase.
ST glycosylation inhibitor **antitumor** hydroxymethylglutaryl CoA reductase; **tunicamycin antitumor** hydroxymethylglutaryl CoA reductase
IT **Neoplasm inhibitors**
(glycosidation inhibitors as)
IT Cell cycle
Deoxyribonucleic acid formation
(of virus-transformed cells, glycosidation inhibitors effect on)
IT Glycosidation
(N-linked, inhibitors of, **neoplasm** inhibition by)
IT 57-88-5, Cholesterol, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, by virus-transformed cells, **tunicamycin** effect on)
IT **11029-02-0, Dolichol**
RL: BIOL (Biological study)
(**neoplasm** inhibition by **tunicamycin** reversal by)
IT 9025-89-2, E.C. 3.1.2.5
RL: PROC (Process)
(of virus-transformed cells, **tunicamycin** inhibition of)
IT **11089-65-9, Tunicamycin** 72741-87-8, Swainsonine
79831-76-8, Castanospermine
RL: BIOL (Biological study)
(proliferation and hydroxymethylglutaryl-CoA reductase activity of virus-transformed cells response to)
IT 2140-46-7, 25-Hydroxycholesterol
RL: BIOL (Biological study)
(virus-transformed **cells proliferation** inhibition by, **dolichol** effect on)
IT **11029-02-0, Dolichol**
RL: BIOL (Biological study)
(**neoplasm** inhibition by **tunicamycin** reversal by)
RN 11029-02-0 HCAPLUS
CN Dolichol (7CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(proliferation and hydroxymethylglutaryl-CoA reductase activity of

virus-transformed cells response to)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1988:35322 HCAPLUS
DN 108:35322
TI The relationship of N-linked glycosylation and heavy chain-binding protein association with the secretion of glycoproteins
AU Dorner, Andrew J.; Bole, David G.; Kaufman, Randal J.
CS Genet. Inst., Cambridge, MA, 02140, USA
SO Journal of Cell Biology (**1987**), 105(6, Pt. 1), 2665-74
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB The relation of N-linked glycosylation and assocn. of heavy chain-binding protein (BiP) to the secretion of **factor VIII** (FVIII), von Willebrand factor (vWF), and tissue plasminogen activator (tPA) was studied in CHO cells. FVIII has a heavily glycosylated region contg. 20 clustered potential N-linked glycosylation sites. A significant proportion of FVIII was detected in a stable complex with BiP and not secreted. Deletion of the heavily glycosylated region resulted in reduced assocn. with BiP and more efficient secretion. **Tunicamycin** treatment of cells producing this deleted form of FVIII resulted in stable assocn. of unglycosylated FVIII with BiP and inhibition of efficient secretion. The vWF contains 17 potential N-linked glycosylation sites scattered throughout the mol. The vWF was transiently assocd. with BiP and efficiently secreted, demonstrating that CHO cells are competent to secrete a highly glycosylated protein. The tPA has 3 utilized N-linked glycosylation sites, exhibited low level assocn. with BiP, and was efficiently secreted. Disruption of N-linked glycosylation of tPA by either site-directed mutagenesis or **tunicamycin** treatment resulted in reduced levels of secretion and increased assocn. with BiP. This effect was enhanced by high levels of tPA expression. The glycosylation state and extent of assocn. with BiP could be correlated with secretion efficiency.
ST glycoprotein secretion glycosidation; protein heavy chain binding glycoprotein secretion
IT Animal cell
(glycoprotein secretion by, N-linked glycosidation and heavy chain-binding protein assocn. with)
IT Glycosidation
(N-linked, of proteins, heavy chain-binding protein assocn. and glycoprotein secretion in relation to)
IT Proteins, specific or class
RL: BIOL (Biological study)
(Ig heavy-chain-binding, glycoprotein secretion in relation to protein N-linked glycosidation and)
IT Biological transport
(secretion, of glycoproteins, N-linked glycosidation and heavy chain-binding protein assocn. in relation to)
IT **109319-16-6**, Von Willebrand Factor **113189-02-9**
RL: BIOL (Biological study)
(secretion of, N-glycosidation and heavy chain-binding protein assocn. with)
IT 105913-11-9, Plasminogen activator
RL: BIOL (Biological study)
(tissue-type, secretion of, N-linked glycosidation and heavy chain-binding protein assocn. with)
IT **109319-16-6**, Von Willebrand Factor **113189-02-9**

RL: BIOL (Biological study)
(secretion of, N-glycosidation and heavy chain-binding protein assocn. with)
RN 109319-16-6 HCAPLUS
CN Blood-coagulation factor VIII, von Willebrand's (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 113189-02-9 HCAPLUS
CN Blood-coagulation factor VIII, procoagulant (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1987:509878 HCAPLUS
DN 107:109878
TI Protein glycosylation and the expression of muscarinic receptors of N4TG1 **neuroblastoma** cells
AU Ahmad, Ateeq; Chiang, Peter K.
CS Dep. Appl. Biochem., Walter Reed Army Inst. Res., Washington, DC, 20307-5100, USA
SO Membr. Proteins, Proc. Membr. Protein Symp. (**1987**), Meeting Date 1986, 611-17. Editor(s): Goheen, Steven C. Publisher: Bio-Rad Lab., Richmond, Calif.
CODEN: 56DMAM
DT Conference
LA English
CC 2-8 (Mammalian Hormones)
AB Expts. were conducted to det. whether active glycosylation of proteins in N4TG1 **neuroblastoma** cells could affect the expression of muscarinic acetylcholine receptors (mAChR) on the cell surface. In the presence of **tunicamycin** and monensin, N-linked glycosylation of proteins in the N4TG1 cells was inhibited, as measured by the incorporation of [3H]**glucosamine** or [14C]mannose into proteins. At the concns. of **tunicamycin** and monensin used, the glycosylation of proteins after 3 h was drastically reduced, but the no. of mAChR in the cells was not altered. The apparent lack of effect within a short incubation period could be attributed to the presence of preformed oligosaccharide **dolichol** readily available for N-glycosylation or the slow turnover of mAChR. However, after 24 h, **tunicamycin** (0.05 .mu.g/mL) caused a decrease in the no. of mAChR by 17% without having any effect on protein synthesis. Therefore, de novo glycosylation of proteins may be required for the expression of mAChR receptors on the N4TG1 **neuroblastoma** cell surface.
ST muscarinic receptor neuron protein glycosylation
IT Proteins, biological studies
RL: RCT (Reactant); RACT (Reactant or reagent)
(glycosidation of, muscarinic receptor expression in neurons in relation to)
IT Glycosidation
(of proteins, muscarinic receptor expression in neurons in relation to)
IT Receptors
RL: BIOL (Biological study)
(muscarinic, of neurons, protein glycosidation in relation to)

L124 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1987:136839 HCAPLUS
DN 106:136839
TI The effect of **tunicamycin** on target cell susceptibility to natural killer cell **cytotoxicity**
AU Nose, M.; Gidlund, M.; Hosein, Z.; Axberg, I.; Wigzell, H.; Yogeeswaran, G.
CS Dep. Immunol., Karolinska Inst., Stockholm, S-104 01, Swed.
SO Scandinavian Journal of Immunology (**1987**), 25(2), 149-57

CODEN: SJIMAX; ISSN: 0300-9475
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB The authors investigated the effect of the glycosylation-inhibitor **tunicamycin**, which acts by blocking the **dolichol** -dependent asparagine-linked glycosylation pathway, on natural killer (NK) cell cytolysis of target cells. Using several different **tumor** cell lines it was concluded that: (a) asparagine-linked carbohydrate chains do not contribute directly to NK susceptibility, (b) induced differentiation may or may not be linked with a change in NK susceptibility, and (c) secondary changes caused by **tunicamycin** treatment may lead to alterations in the gangliosides, a finding that is pos. correlated with decreased NK susceptibility.
ST natural killer lymphocyte cytolysis carbohydrate
IT Carbohydrates and Sugars, biological studies
RL: BIOL (Biological study)
(asparagine-linked, in target cell susceptibility to cytolysis by natural killer lymphocytes)
IT Cytolysis
(by natural killer lymphocytes, carbohydrates in)
IT Glycosidation
Gangliosides
RL: BIOL (Biological study)
(in natural killer lymphocyte **cytotoxicity**)
IT Lymphocyte
(natural killer, cytolysis by, target cell susceptibility to, carbohydrates in)

L124 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1984:627589 HCAPLUS
DN 101:227589
TI N-Glycosylation of nascent proteins early in the prereplicative phase constitutes a process for controlling animal **cell proliferation**
AU De Asua, Luis Jimenez; Poskocil, Stanislava; Foecking, M. Katherine; Otto, Angela M.
CS Friedrich Miescher-Inst., Basel, CH-4002, Switz.
SO Hormones and Cell Regulation (**1984**), 8, 37-51
CODEN: HCREDN; ISSN: 0166-0969
DT Journal
LA English
CC 13-3 (Mammalian Biochemistry)
AB DNA synthesis initiated by mitogens in quiescent Swiss 3T3 cells in culture is inhibited when the 1st steps of glycoprotein formation are blocked by specific inhibitors. Apparently glycoprotein formation is essential for the transition of cells into S phase. When hydroxymethylglutaryl-CoA reductase (which forms mevalonate at the beginning of the pathway leading to **dolichol** formation) is inhibited by mevinolin, the initiation of DNA synthesis stimulated by epidermal growth factor or prostaglandin F2.alpha. (in the presence or absence of insulin) or fetal calf serum is inhibited. Mevinolin appears specific for this enzyme, since mevalonolactone overcomes the inhibition by mevinolin. **Tunicamycin**'s inhibition of the initial step of the synthesis of glycoprotein linked to **dolichol** inhibits the initiation of DNA synthesis due to the effect of serum or other mitogens. The kinetics of the action of **tunicamycin** suggest that glycoprotein formation during the 1st 8 h of latency is essential for the later formation of DNA. A working hypothesis is presented which links mitogenic events in the environs of the cell membrane to later nuclear events.
ST DNA glycoprotein formation mitogen; protein glycosylation fibroblast S phase; mevalonate formation DNA cell growth

IT Blood serum
(DNA formation by fibroblast stimulation by, glycoprotein formation in relation to)
IT Mitogens
(DNA formation stimulation by, in fibroblast, glycoprotein formation in relation to)
IT Deoxyribonucleic acid formation
(by fibroblast, cell growth and glycoprotein formation in relation to)
IT Glycosidation
(of proteins, by fibroblast, cell growth and DNA formation in relation to)
IT Fibroblast
(3T3, DNA and glycoprotein formation by, cell growth in relation to)
IT Cell cycle
(S-phase, glycoprotein formation by fibroblast in regulation of)
IT 9028-35-7
RL: BIOL (Biological study)
(DNA and glycoprotein formation and cell growth by fibroblast in relation to)
IT 551-11-1
RL: BIOL (Biological study)
(DNA formation by fibroblast stimulation by, glycoprotein formation in relation to)
IT 9004-10-8, biological studies
RL: BIOL (Biological study)
(DNA formation stimulation by mitogens and, fibroblast growth and glycoprotein formation in relation to)
IT 150-97-0
RL: FORM (Formation, nonpreparative)
(formation of, by fibroblast, DNA and glycoprotein formation and cell growth in relation to)

L124 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1984:608463 HCAPLUS
DN 101:208463
TI Alterations induced by glucose deprivation and **tunicamycin** in the kinetic parameters of hexose transport in hybrid cells
AU White, M. K.; Bramwell, M. E.; Harris, H.
CS Sir William Dunn Sch. Pathol., Univ. Oxford, Oxford, OX1 3RE, UK
SO Journal of Cell Science (**1984**), 68, 257-70
CODEN: JNCSAI; ISSN: 0021-9533
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13
AB Matched pairs of **malignant** and **nonmalignant** hybrid cells were compared in their response to glucose deprivation and to **tunicamycin** (which blocks the **dolichol** pyrophosphate-mediated glycosylation of glycoproteins). Glucose deprivation induced an increase in the max. velocity in the **malignant** cells, but not in the **nonmalignant** cells. Km Of hexose uptake was largely unchanged by glucose deprivation except in the case of one **melanoma** deriv., PG19 G-, which showed a large increase in Km when deprived of glucose. **Tunicamycin** increased Km of hexose uptake in both **malignant** and **nonmalignant** cell lines. It is therefore possible that the Km of hexose uptake is affected by the extent of glycosylation of .gtoreq.1 of the cell membrane glycoproteins.
ST hexose transport **neoplastic** normal cell; glucose deprivation hexose transport cell; glycoprotein glycosylation hexose transport cell
IT Cell membrane
(glycoproteins of, of **neoplastic** and normal cells, hexose transport in relation to)

IT Glycoproteins
RL: RCT (Reactant); RACT (Reactant or reagent)
(glycosylation of, of **neoplastic** and normal cells, hexose transport in relation to)
IT **Melanoma**
(hexose transport by PG19 G-, glucose deprivation effect on, glycoprotein glycosylation in relation to)
IT **Neoplasm, metabolism**
(hexose transport by, glucose deprivation and glycoprotein glycosylation effects on)
IT Animal cell
(hexose transport by, glucose deprivation effect on, glycoprotein glycosylation role in)
IT Biological transport
(of hexoses, by **neoplastic** and normal cells, glucose deprivation and glycoprotein glycosylation effects on)
IT Hexoses
RL: BIOL (Biological study)
(transport of, by **neoplastic** and normal cells, glucose deprivation and glycoprotein glycosylation effects on)
IT 50-99-7, biological studies
RL: BIOL (Biological study)
(deprivation of, hexose transport by **neoplastic** and normal cells responses to)
IT 37247-98-6
RL: BIOL (Biological study)
(glycoprotein glycosylation mediated by, in **neoplastic** and normal cells, hexose transport in relation to)

L124 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1984:507952 HCAPLUS
DN 101:107952
TI Influence of effectors of the complex-type-oligosaccharide biosynthesis on the formation of proteokeratan sulfate in bovine **cornea**
AU Ziegler, Clemens; Mersmann, Guenther
CS Physiol. Chem. Inst., Univ. Muenster, Muenster, D-4400, Fed. Rep. Ger.
SO Biochimica et Biophysica Acta (**1984**), 799(3), 203-8
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB The structural similarity of the inner core of complex-type prosthetic oligosaccharides of N-asparagine glycoproteins and of the linkage region between the polysaccharide part and the protein chain of **cornea** proteokeratan sulfate makes their biosynthesis via a common route an attractive hypothesis. To test this, a tissue culture system was established to det. the rate of proteokeratan sulfate biosynthesis in bovine **cornea** and to measure the influence of several effectors of the **dolichol** path on this rate. Addn. of **dolichyl** phosphate enhanced the formation of proteokeratan sulfate. **Tunicamycin**, 2-deoxy-D-glucose, bromoconduritol, and deoxynorjirimycin inhibited this process. Swainsonine probably led to the formation of a keratan sulfate with hybrid structure. The results support that the linkage region of **cornea** proteokeratan sulfate is synthesized via the assembly of a glucosylated **dolichyl** pyrophosphoryl oligosaccharide, its transfer to protein, and subsequent processing by glycosidases.
ST proteokeratin sulfate formation **cornea**; oligosaccharide complex proteokeratin sulfate formation
IT Eye, metabolism
(**cornea**, proteokeratan sulfate formation by)
IT Mucopolysaccharides, biological studies
RL: FORM (Formation, nonpreparative)

(proteokeratan sulfates, formation of, by **cornea**)
IT 9056-36-4D, proteoglycans contg.
RL: FORM (Formation, nonpreparative)
(formation of, by **cornea**)
IT 12698-55-4
RL: BIOL (Biological study)
(in proteokeratan sulfate formation by **cornea**)
IT 72741-87-8
RL: BIOL (Biological study)
(proteokeratan sulfate formation by **cornea** in relation to)
IT 154-17-6 526-87-4D, bromo derivs. **11089-65-9** 19130-96-2
RL: BIOL (Biological study)
(proteokeratan sulfate formation by **cornea** inhibition by)
IT **11089-65-9**
RL: BIOL (Biological study)
(proteokeratan sulfate formation by **cornea** inhibition by)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1983:436676 HCAPLUS
DN 99:36676
TI Effects of dibutyryl cyclic AMP on the syntheses of **dolichol**-linked saccharides and glycoproteins in cultured **hepatoma** cells. Correlation with the effect on the adhesiveness of the cells
AU Okamoto, Yasushi; Sakai, Hiroshi; Sato, Jiro; Akamatsu, Nobu
CS Sch. Med., St. Marianna Univ., Kawasaki, 213, Japan
SO Biochemical Journal (**1983**), 212(3), 859-67
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
CC 14-1 (Mammalian Pathological Biochemistry)
AB When **hepatoma** cells (AH 70Btc, Clone 10-5) were cultured in the presence of 1 mM-dibutyryl cyclic AMP for 2 days, the incorporation of [14C]**glucosamine** into protein was increased over 2-fold. At the same time, dibutyryl cyclic AMP increased the incorporation of [14C]**glucosamine** into **dolichol**-linked N-**acetylglucosamine** and N,N'-diacetylchitobiose about 1.5-fold and into **dolichol**-linked oligosaccharides about 3-fold. Anal. of cellular glycoproteins by SDS-polyacrylamide-gel electrophoresis after redn. showed that dibutyryl cyclic AMP specifically enhanced the glycosylation of a fibronectin-like glycoprotein with an apparent mol. wt. of 220,000 and 2 other high-mol.-wt. glycoproteins (apparent mol. wts. 270,000 and 185,000). Increased glycosylation of the glycoproteins with mol. wts. of 220,000 and 185,000 was linked to increased synthesis of the polypeptide portion. Dibutyryl cyclic AMP also enhanced the adhesiveness of AH 70Btc cells to glass surfaces. Both the effects on the glycosylation pathway and on adhesiveness of cells were reversed by further treatment of the cells with 1 .mu.g of **tunicamycin**/mL. Thus, dibutyryl cyclic AMP increased the synthesis of **dolichol**-linked oligosaccharides and N-glycosylation of proteins in AH 70Btc cells. The enhancement of adhesiveness may be mediated by the increased synthesis of **dolichol**-linked oligosaccharides and also may be related to the increased synthesis of fibronectin.
ST **hepatoma** glycoprotein adhesiveness dibutyryl cAMP; **dolichol** oligosaccharide **hepatoma** dibutyryl cAMP
IT Oligosaccharides
RL: BIOL (Biological study)
(**dolichol**-linked, of **hepatoma**, dibutyryl cyclic AMP effect on, cell adhesiveness in relation to)
IT Fibronectins

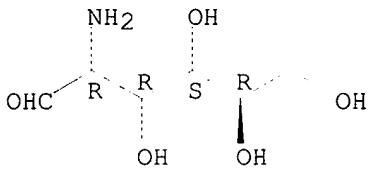
Glycoproteins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(of **hepatoma**, dibutyryl cyclic AMP effect on, cell adhesiveness in relation to)
IT Liver, **neoplasm**
(**hepatoma**, **dolichol**-linked oligosaccharides and glycoproteins of, dibutyryl cyclic AMP effect on, cell adhesiveness in relation to)
IT 362-74-3
RL: BIOL (Biological study)
(**dolichol**-linked oligosaccharides and glycoproteins of **hepatoma** response to, cell adhesiveness in relation to)

L124 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1983:191409 HCAPLUS
DN 98:191409
TI Biochemical effects and therapeutic potential of **tunicamycin** in murine L1210 leukemia
AU Morin, Michael J.; Bernacki, Ralph J.
CS Grace Cancer Drug Cent., Roswell Park Mem. Inst., Buffalo, NY, 14263, USA
SO Cancer Research (**1983**), 43(4), 1669-74
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
CC **1-6** (Pharmacology)
AB **tunicamycin** [**11089-65-9**], An antibiotic which specifically inhibits the **dolichol**-mediated synthesis of glycoproteins, significantly decreased the incorporation of tritiated D-mannose [3458-28-4] and D-**glucosamine** [**3416-24-8**] into L1210 ascites leukemia cell glycoproteins at concns. which affected the biosynthesis of proteins minimally. Mice receiving inoculations of L1210 cells pretreated with 10 .mu.M **tunicamycin** in vitro survived nearly twice as long as did mice receiving implants of untreated **tumor** cells. A nonlethal dose of X-irradn. (350 rads) to mice 24 h prior to receiving their inoculation of **tunicamycin**-treated L1210 cells prevented this increase in life span. Thirty-eight percent of the long-term surviving mice which received 1 .times. 105 L1210 cells pretreated with 10 .mu.M **tunicamycin** in vitro were then resistant to a subsequent challenge with 106 untreated L1210 ascites cells. Direct i.p. administration of **tunicamycin** to mice resulted in potent liver toxicity (50% LD, 2.0 mg/kg) which obviated any therapeutic efficacy when administered to L1210 ascites **tumor** -bearing mice. The administration of nontoxic levels of D-mannose prior to the administration of **tunicamycin** decreased the toxicity of the antibiotic in vivo and, when combined with D-mannose in vitro, exhibited **cytotoxic** additivity in terms of the inhibition of L1210 leukemic cell growth. A therapeutic regimen incorporating a 24-h infusion of the sugar prior to multiple administrations of **tunicamycin** gave evidence of a small therapeutic response in terms of the survival of **tumor**-bearing mice. Thus, **tunicamycin** might be able to alter **tumor** cell growth and immunogenicity provided that host liver toxicity is diminished.
ST **tunicamycin antitumor** liver toxicity; glycoprotein formation **antitumor tunicamycin**
IT Glycoproteins
RL: FORM (Formation, nonpreparative)
(formation of, by **tumor**, **tunicamycin** inhibition of)
IT **Neoplasm inhibitors**
(**tunicamycin** as)
IT Liver, toxic chemical and physical damage
(**tunicamycin** toxicity to, mannose effect on)
IT **11089-65-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antitumor** activity of, liver toxicity in relation to)
IT **3416-24-8**
RL: BIOL (Biological study)
(glycoprotein formation from, in **tumor**, **tunicamycin** inhibition of)
IT 3458-28-4
RL: BIOL (Biological study)
(**tunicamycin antitumor** activity and liver toxicity in relation to)
IT **11089-65-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antitumor** activity of, liver toxicity in relation to)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **3416-24-8**
RL: BIOL (Biological study)
(glycoprotein formation from, in **tumor**, **tunicamycin** inhibition of)
RN 3416-24-8 HCAPLUS
CN D-Glucose, 2-amino-2-deoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L124 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1983:158521 HCAPLUS
DN 98:158521
TI **Tunicamycin** inhibits ganglioside biosynthesis in neuronal cells
AU Guarnaccia, Steven P.; Shaper, Joel H.; Schnaar, Ronald L.
CS Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO Proceedings of the National Academy of Sciences of the United States of America (**1983**), 80(6), 1551-5
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 13-7 (Mammalian Biochemistry)
AB The antibiotic, **tunicamycin** (I), blocks the transfer of **acetylglucosamine** 1-phosphate from UDP-acethylglucosamine (II) to **dolichol** phosphate, thereby blocking the synthesis of N-linked oligosaccharide chains on glycoproteins. Its effect on the biosynthesis of gangliosides has not previously been reported. I caused a 70-80% redn. in incorporation of [3H]**glucosamine** into gangliosides and neutral glycosphingolipids of the **neuroblastoma-glioma** hybrid cell line NG 108-15 at I concns. that caused a 90% redn. of the radiolabel incorporation into glycoproteins. The effect of I on ganglioside biosynthesis was apparent after only 4 h of incubation, and max. inhibition was seen within 6 h. When control or I-treated (5 .mu.g/mL) cells were collected and fractionated to sep. glycoproteins, neutral glycosphingolipids, gangliosides, and nucleotide sugar-precursor

pools, the following results were obtained. II and UDP-acetylgalactosamine pool sizes increased >3-fold, and specific activities decreased 50% upon treatment with I. When cor. for this value, the percentage inhibition of **glucosamine** incorporation into various glycoconjugates by I in these cells was 82% for glycoproteins, 54% for neutral glycosphingolipids, and 50% for gangliosides. The different gangliosides were affected differentially, with the most striking inhibition apparent in GM3 biosynthesis, which was decreased 78% in the presence of I. Thus, the effects of I on glycosphingolipids as well as on glycoproteins must be considered when interpreting its effect on intact cells and organisms.

ST ganglioside formation **neuroblastoma glioma** **tunicamycin**

IT Gangliosides
Glycoproteins
RL: FORM (Formation, nonpreparative)
(formation of, by **neuroblastoma-glioma** hybrid cells, **tunicamycin** inhibition of)

IT Glycosidation
(in ganglioside formation, by **neuroblastoma-glioma** hybrid cells, **tunicamycin** inhibition of)

IT Glycolipids
RL: BIOL (Biological study)
(neutral, formation of, by **neuroblastoma-glioma** hybrid cells, **tunicamycin** inhibition of)

IT Neuroglia
(**neoplasm, glioma, -neuroblastoma** hybrid, ganglioside formation by, **tunicamycin** inhibition of)

IT Nerve, **neoplasm**
(**neuroblastoma, -glioma** hybrid, ganglioside formation by, **tunicamycin** inhibition of)

IT Glycosphingolipids
RL: FORM (Formation, nonpreparative)
(neutral, formation of, by **neuroblastoma-glioma** hybrid cells, **tunicamycin** inhibition of)

IT 19600-01-2 37758-47-7 54827-14-4
RL: FORM (Formation, nonpreparative)
(formation of, by **neuroblastoma-glioma** hybrid cells, **tunicamycin** inhibition of)

IT **11089-65-9**
RL: BIOL (Biological study)
(ganglioside formation by **neuroblastoma-glioma** hybrid cells inhibition by)

IT 528-04-1 7277-98-7
RL: BIOL (Biological study)
(of **neuroblastoma-glioma** hybrid cells, **tunicamycin** effect on, ganglioside formation inhibition in relation to)

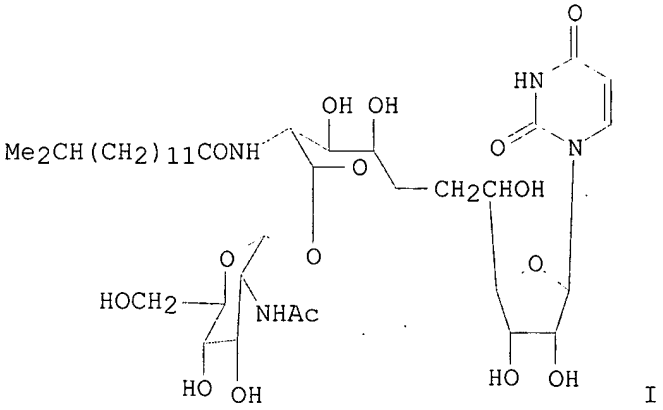
IT **11089-65-9**
RL: BIOL (Biological study)
(ganglioside formation by **neuroblastoma-glioma** hybrid cells inhibition by)

RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1983:241 HCAPLUS
DN 98:241
TI Inhibition of protein glycosylation and selective **cytotoxicity** toward virally transformed fibroblasts caused by B3-**tunicamycin**
AU Duksin, Dan; Seiberg, Miri; Mahoney, Walter C.

CS Dep. Biophys., Weizmann Inst. Sci., Rehovot, IL-76-100, Israel
SO European Journal of Biochemistry (**1982**), 129(1), 77-80
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
CC **1-6** (Pharmacology)
GI



I

AB The biol. effect of B3-**tunicamycin** (I) [**76544-50-8**], the only known homolog of **tunicamycin** which contains a satd. fatty-acid side chain, was examd. in chick embryo fibroblasts, a mouse fibroblastic line (3T3), and a virally transformed mouse fibroblastic line (SV 40-3T3). This homolog inhibited the transfer of N-**acetylglucosamine** 1-phosphate from UDP-N-**acetylglucosamine** to **dolichyl** phosphate, catalyzed by microsomes from chick liver or from cultured mouse fibroblasts. B3-**tunicamycin** also inhibited the incorporation of mannose into glycoproteins synthesized by chick or mouse fibroblasts. Incorporation of the amino acids proline and tyrosine was inhibited by B3-**tunicamycin** to a lesser extent than the incorporation of mannose. The mannose incorporation into glycoproteins synthesized by virally transformed cells was inhibited by B3-**tunicamycin** to a higher degree than what was achieved in the nontransformed lines or in the chick primary fibroblasts. When the activity of B3-**tunicamycin** as an inhibitor of protein glycosylation was compared to other homologs of **tunicamycin**, it was found to be the most active. This homolog caused complete inhibition of protein glycosylation at a concn. of 50 ng/mL in chick and mouse fibroblasts and at a concn. of 10 ng/mL in transformed mouse fibroblasts. When the **cytotoxic** activities of **tunicamycin** homologs were examd. on nontransformed and virally transformed 3T3 cells, it was found that B3-**tunicamycin** displayed the highest selective **cytotoxicity** toward the transformed cells. When transformed fibroblasts (105 cells/plate) were treated with B3-**tunicamycin** (100 ng/mL) for 48 h, complete cell death was obsd. The visibility and the proliferative activity of the nontransformed fibroblast were normal even when treated with concns. up to 500 ng/mL of B3-**tunicamycin** . This suggests that B3-**tunicamycin** may be a suitable candidate for studies of **tumor** growth in animals.

ST B3 **tunicamycin** transformed cell **cytotoxicity**; protein glycosylation B3 **tunicamycin cytotoxicity**
IT **Cytotoxic** agents
(B3-**tunicamycin**)

IT Proteins
RL: RCT (Reactant); RACT (Reactant or reagent)
(glycosylation of, B3-**tunicamycin** inhibition of, **cytotoxicity** in relation to)
IT Glycosidation
(of proteins, B3 **tunicamycin** inhibition of, **cytotoxicity** in relation to)
IT **76544-50-8**
RL: BIOL (Biological study)
(protein glycosylation inhibition by, **cytotoxicity** in relation to)
IT **76544-50-8**
RL: BIOL (Biological study)
(protein glycosylation inhibition by, **cytotoxicity** in relation to)
RN 76544-50-8 HCAPLUS
CN Tunicamycin B3 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1982:576671 HCAPLUS
DN 97:176671
TI Effect of **tunicamycin** on receptors for **tumor** promoters
AU Solanki, V.; Logani, M. K.; Slaga, T. J.
CS Oak Ridge Grad. Sch. Biomed. Sci., Univ. Tennessee, Oak Ridge, TN, 37830, USA
SO Cancer Letters (Shannon, Ireland) (**1982**), 16(3), 319-25
CODEN: CALEDQ; ISSN: 0304-3835
DT Journal
LA English
CC 4-6 (Toxicology)
Section cross-reference(s): **1**, 14
AB A progressive decline in the specific binding of 20-3H-labeled phorbol 12,13-dibutyrate ([3H]PDBu) [37558-16-0] and glycoprotein synthesis was obsd. following treatment of primary mouse epidermal cells with **tunicamycin** [**11089-65-9**], a specific inhibitor of **dolichol**-mediated glycosylation. Following 18 h of treatment, the specific binding of [3H]PDBu was reduced to 33-56% of the control value. The total protein synthesis detd. by leucine incorporation into acid-insol. material was not altered by this antibiotic drug. Apparently, the receptor for phorbol diesters is, or is functionally linked to, a glycoprotein on the cell surface.
ST **tunicamycin** receptor **tumor** promoter
IT Receptors
RL: BIOL (Biological study)
(for **tumor** promoters, **tunicamycin** effect on, glycoprotein formation in relation to)
IT Glycoproteins
RL: FORM (Formation, nonpreparative)
(formation of, **tunicamycin** effect on receptor for **tumor** promoter in relation to)
IT Epidermis
(phorbol dibutyrate binding by, **tunicamycin** effect on)
IT **Neoplasm**
(promoters, **tunicamycin** effect on receptors for)
IT 37558-16-0
RL: BIOL (Biological study)
(binding of, by epidermis receptor, **tunicamycin** effect on)
IT **11089-65-9**
RL: BIOL (Biological study)
(receptors for **tumor** promoters response to)
IT **11089-65-9**

RL: BIOL (Biological study)
(receptors for **tumor** promoters response to)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1982:556513 HCAPLUS
DN 97:156513
TI Selection of **tunicamycin**-resistant Chinese **hamster** ovary cells with increased N-acetylglucosaminyltransferase activity
AU Criscuolo, Barbara a.; Krag, Sharon S.
CS Sch. Hyg. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO Journal of Cell Biology (**1982**), 94(3), 586-91
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
CC **1-12** (Pharmacology)
Section cross-reference(s): 13
AB Chinese hamster ovary (CHO) cells resistant to **tunicamycin** (TM) [**11089-65-9**] were isolated by a stepwise selection procedure with progressive increments of TM added to the medium. TM inhibits asparagine-linked glycoprotein biosynthesis by blocking the transfer of N-**acetylglucosamine**-1-phosphate from UDP-N-**acetylglucosamine** to the lipid carrier. The TM-resistant cells exhibited a 200-fold increase in their LD50 for TM and were morphol. distinct from the parental cells. The rate of asparagine-linked glycoprotein biosynthesis was the same for wild-type and TM-resistant cells. Membrane prepns. from TM-resistant cells cultured for 16 days in the absence of TM had a 15-fold increase in the specific activity of the UDP-N-**acetylglucosamine** :**dolichol** phosphate N-**acetylglucosamine** -1-phosphatetransferase [**70431-08-2**] as compared to membranes of wild-type cells. The products of the in vitro assay were N-acetylglucosaminylpyrophosphoryl-lipid and N,N'-diacetylchitobiosylpyrophosphoryl-lipid for membranes from both TM-resistant and wild-type cells. The transferase activity present in membrane prepns. from wild-type or TM-resistant cells was inhibited by comparable levels of TM. The data presented are consistent with overprodn. of enzyme as the mechanism of resistance in these variant CHO cells.
ST **tunicamycin** resistant ovary cell selection; acetylglucosaminyltransferase cell **tunicamycin** resistance
IT Drug resistance
(**cytotoxic**, to **tunicamycin**, of ovary cells)
IT Ovary
(**tunicamycin**-resistant cells of, selection of, acetylglucosaminyltransferase activity in relation to)
IT **70431-08-2**
RL: BIOL (Biological study)
(of **tunicamycin**-resistant ovary cells)
IT **11089-65-9**
RL: BIOL (Biological study)
(ovary cells resistant to, selection of, acetylglucosaminyltransferase activity in relation to)
IT **70431-08-2**
RL: BIOL (Biological study)
(of **tunicamycin**-resistant ovary cells)
RN 70431-08-2 HCAPLUS
CN Acetylglucosamine-1-phosphotransferase, uridine diphosphoacetylglucosamine-dolichyl phosphate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **11089-65-9**
RL: BIOL (Biological study)
(ovary cells resistant to, selection of, acetylglucosaminyltransferase activity in relation to)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L124 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1982:404002 HCAPLUS
DN 97:4002
TI Effect of **tunicamycin** on insulin binding and on proteoglycan synthesis and distribution in Swarm rat **chondrosarcoma** cell cultures
AU Stevens, Richard L.; Schwartz, Lawrence B.; Austen, K. Frank; Lohmander, L. Stefan; Kimura, James H.
CS Dep. Med., Harvard Med. Sch., Boston, MA, 02115, USA
SO Journal of Biological Chemistry (**1982**), 257(10), 5745-50
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
Section cross-reference(s): 2
AB **Tunicamycin** (I), an inhibitor of **dolichol**-diphospho-N-**acetylglucosamine** formation and hence an inhibitor of N-linked oligosaccharide biosynthesis, suppressed total proteoglycan synthesis by Swarm rat **chondrosarcoma** chondrocytes without affecting the size of the proteoglycan mol., its secretion from the cell, or its ability to be retained in the extracellular matrix. In addn., I did not substantially alter the ability of the chondrocytes to polymerize glycosaminoglycan onto an exogenous .beta.-D-xyloside acceptor. A secondary effect of I suppression of proteoglycan synthesis was that a lesser amt. of newly synthesized proteoglycan diffused from the extracellular matrix into the culture medium. The ability of exogenous hyaluronic acid and proteoglycan to increase the percentage of newly synthesized 35S-labeled proteoglycan in the medium in I-treated cultures indicates that matrix retention of 35S-labeled proteoglycan is related to the total extracellular uronic acid content rather than to the presence or absence of mannose oligosaccharides bound to the proteoglycan mol. These noncytotoxic concns. of I (33-333 ng/mL) decreased [3H]mannose incorporation to the same extent that they decreased total [35S]sulfate and [3H]serine incorporation and caused the chondrocyte to synthesize and secrete a species of .beta.-hexosaminidase that was mannose-deficient as assessed by its failure to bind to Con A. The addnl. finding of decreased insulin binding to I-treated **chondrosarcoma** chondrocytes suggested that the inhibition of proteoglycan synthesis was due to diminution of receptors which respond to stimulatory hormones.
ST **chondrosarcoma** proteoglycan formation oligosaccharide; insulin binding **chondrosarcoma** oligosaccharide
IT Protein formation
(by **chondrosarcoma** cells, N-linked oligosaccharide formation in relation to)
IT Oligosaccharides
RL: BIOL (Biological study)
(N-linked, formation of, insulin binding and sulfated proteoglycan formation and secretion by **chondrosarcoma** cells in relation to)
IT **Sarcoma**
(chondro-, insulin binding and sulfated proteoglycan formation and secretion by, N-linked oligosaccharide formation in relation to)
IT Mucopolysaccharides, compounds
RL: BIOL (Biological study)

(proteoglycans, sulfated, formation and secretion of, by **chondrosarcoma** cells, N-linked oligosaccharide formation in relation to)

IT 9004-10-8, biological studies
RL: BIOL (Biological study)
(**chondrosarcoma** cell binding of, N-linked oligosaccharide formation in relation to)

IT 9027-52-5
RL: BIOL (Biological study)
(formation and secretion of, by **chondrosarcoma** cells, N-linked oligosaccharide formation in relation to)

IT 9004-61-9
RL: BIOL (Biological study)
(sulfated proteoglycan formation and secretion by **chondrosarcoma** cells in response to)

L124 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1981:57983 HCAPLUS
DN 94:57983
TI Interferon treatment inhibits glycosylation of a viral protein
AU Maheshwari, Radha K.; **Banerjee, Dipak K.**; Waechter, Charles J.; Olden, Kenneth; Friedman, Robert M.
CS Lab. Exp. Pathol., Natl. Inst. Arthritis Metab. Dis., Bethesda, MD, 20205, USA
SO Nature (London, United Kingdom) (1980), 287(5781), 454-6
CODEN: NATUAS; ISSN: 0028-0836
DT Journal
LA English
CC 1-4 (Pharmacodynamics)
Section cross-reference(s): 15
AB **Tunicamycin** (0.5 or 1.0 .mu.g/mL) and interferon (30 international mouse ref. units/mL) reduced infectious virus titer in vesicular stomatitis virus (VSV) released from L cells by 10-80-fold and 200-fold, resp., decreased the amts. of glycoprotein and membrane protein in released VSV, and inhibited an early step in the formation of asparagine-linked oligosaccharide chains, viz. the incorporation by membrane prepns. from treated cells of N-**acetylglucosamine** into glycolipids with the properties of **dolichol** derivs. The latter are precursors of **dolichol**-bound oligosaccharide lipid intermediates in protein glycosylation. If glycosylation of asparagine residues in viral membrane glycoproteins is crit. for the assembly of infectious particles of some viruses, inhibition of the enzymic transfer of N-**acetylglucosamine** 1-phosphate from the nucleotide deriv. to **dolichol** phosphate could be an effective means of impeding viral prodn.
ST interferon virus protein glycosylation
IT Mucopolysaccharides, compounds
RL: BIOL (Biological study)
(**dolichol** complexes, interferon inhibition of viral glycoprotein formation in relation to)

IT Interferons
RL: BIOL (Biological study)
(viral protein glycosylation inhibition by, **dolichol**-bound glycolipid intermediate in relation to)

IT Glycoproteins
RL: BIOL (Biological study)
(viral, formation of, interferon inhibition of, **dolichol**-bound glycolipid intermediate in relation to)

IT Proteins
RL: BIOL (Biological study)
(viral, glycosylation of, interferon inhibition of, **dolichol**-bound glycolipid intermediate in relation to)

IT Virus, animal

(vesicular stomatitis, glycoprotein formation by, interferon inhibition of, **dolichol**-bound glycolipid intermediate in relation to)
IT 56938-89-7
RL: BIOL (Biological study)
(as viral glycoprotein-formation intermediate, interferon antiviral activity in relation to)

L124 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2003 ACS
AN 1979:551124 HCAPLUS
DN 91:151124
TI Selective **cytotoxicity** of **tunicamycin** for transformed cells
AU Olden, Kenneth; Pratt, Robert M.; Yamada, Kenneth M.
CS Lab. Mol. Biol., Natl. Cancer Inst., Bethesda, MD, 20014, USA
SO International Journal of Cancer (**1979**), 24(1), 60-6
CODEN: IJCNAW; ISSN: 0020-7136
DT Journal
LA English
CC **1-4** (Pharmacodynamics)
AB The effects of **tunicamycin** [**11089-65-9**], an inhibitor of **dolichol** pyrophosphate-dependent glycosylation of proteins, on the viability of transformed and nontransformed fibroblasts in culture were studied. A low concn. of **tunicamycin** (0.05 .mu.g/mL or 5 x 10-8M) was **cytotoxic** toward a variety of transformed cell lines, including virally or chem. transformed fibroblasts from chick embryo, rat kidney, human lung, and mouse. The corresponding nontransformed cell lines were resistant to the same and a 10-fold higher concn. of **tunicamycin**. However, transformed permanent cell lines were also resistant to **tunicamycin**. The relationship between transformation and **tunicamycin cytotoxicity** was strengthened by the finding that chick embryo fibroblasts infected by the temp.-sensitive viral mutants ts68 or T5 were killed by the drug only at the temp. at which transformation is expressed. The LD50 for sensitive transformed cell lines ranged from 0.02 to 0.034 .mu.g-mL **tunicamycin**. Maximal **cytotoxic** effects to transformed cells were produced at **tunicamycin** concns. which only slightly inhibited protein synthesis in nontransformed cells (17-22% in 24 h). There was a good correlation between the susceptibility of transformed cells to **tunicamycin cytotoxicity** and their sensitivity to **tunicamycin** inhibition of protein glycosylation, 2-deoxy-D-glucose transport, and glucose metab. These results indicate that **tunicamycin** interferes with some cellular process crit. for the survival of many transformed cells but not of nontransformed cells. Apparently, the **cytotoxicity** of this drug towards transformed cells may result from impaired rates of nutrient transport, although other mechanisms are possible. **Tunicamycin** may, therefore, be therapeutically useful as an **antitumor** agent to selectively kill certain types of **malignant** cells, while sparing nontransformed cells.
ST **tunicamycin cytotoxicity** transformed cell
IT **Cytotoxic** agents
(**tunicamycin**)
IT **11089-65-9**
RL: PRP (Properties)
(**cytotoxicity** of, for transformed cells)
IT **11089-65-9**
RL: PRP (Properties)
(**cytotoxicity** of, for transformed cells)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d l125 all hitstr tot

L125 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:343834 HCAPLUS
DN 133:217425
TI The effects of glycosylation inhibitors on the proliferation of a Wilms **tumor** cell line
AU Granerus, Marika; Engstrom, Wilhelm
CS Department of Pathology, Swedish University of Agricultural Sciences, Uppsala, S-750 07, Swed.
SO Anticancer Research (**2000**), 20(2A), 689-692
CODEN: ANTRD4; ISSN: 0250-7005
PB International Institute of Anticancer Research
DT Journal
LA English
CC **1-6** (Pharmacology)
Section cross-reference(s): 14
AB We have examd. the effects of different glycosylation inhibitors on the proliferation of a human Wilms **tumor**-derived cell line WCCS-1. It was found that two compds. that specifically inhibit distal steps in the glycosylation chain (swainsonine and castanospermine) only exerted marginal effects on cell multiplication and survival. In contrast, a proximal inhibitor (**tunicamycin**) efficiently increased necrosis in a dose dependent fashion. It is shown that this cell death was accompanied by a marked decrease in the incorporation of **glucosamine**, but rather unexpectedly, only caused a limited inhibition of de novo protein synthesis. Moreover, the entrance into S-phase was virtually unchanged in the cells surviving the exposure to **tunicamycin**. The effects of **tunicamycin** on cell multiplication and survival could not be reversed by concomitant addn. of mevalonate as has been shown in other cell lines. Taken together this data suggests that **tunicamycin** does not operate in a cell cycle-specific manner in Wilms **tumor** cells.
ST glycosylation inhibitor Wilms **tumor** cell cycle
IT Interphase (cell cycle)
(S-phase; glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
IT Kidney, **neoplasm**
(Wilms'; glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
IT Cell cycle
Translation, genetic
(glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
IT Glycosylation
(glycosylation inhibitors effect on wilms **tumor cell proliferation**)
IT **11089-65-9, Tunicamycin** 72741-87-8, Swainsonine
79831-76-8, Castanospermine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
IT **3416-24-8, Glucosamine**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Carlberg, M; Carcinogenesis 1996, V17, P2589 HCAPLUS

(2) DeSantis, R; Biochem Biophys Res Comm 1987, V142, P348 HCAPLUS
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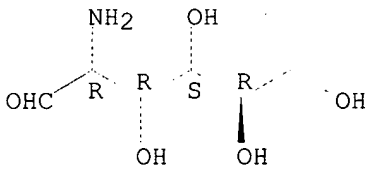
(12) Nishiura, T; Blood 1996, V88, P3546 HCAPLUS
(13) Roberts, J; Cancer Detect Prev 1998, V22, P455 HCAPLUS
(14) Talts, J; Int J Cancer 1993, V54, P868 HCAPLUS
(15) Zetterberg, A; Cell cycle control 1995, P206 HCAPLUS

IT **11089-65-9, Tunicamycin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **3416-24-8, Glucosamine**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(glycosylation inhibitors effect on Wilms **tumor cell proliferation**)
RN 3416-24-8 HCAPLUS
CN D-Glucose, 2-amino-2-deoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L125 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:68979 HCAPLUS
DN 120:68979
TI Effect of **tunicamycin** on the insulin receptor on the surface of human **hepatocarcinoma** cell line SMMC-7721
AU Qi, Weiwei; Chen, Huili
CS Dep. Biochem., Shanghai Med. Univ., Shanghai, 200032, Peop. Rep. China
SO Shengwu Huaxue Zazhi (**1993**), 9(5), 615-19
CODEN: SHZAE4; ISSN: 1000-8543
DT Journal
LA Chinese
CC **1-6** (Pharmacology)
AB **Tunicamycin** is an inhibitor of the synthesis of N-linked oligosaccharide on glycoprotein. It was found that the growth of human **hepatocarcinoma** cell line SMMC-7721 was inhibited by **tunicamycin**, the inhibitory rate was proportional to the dose and the duration of **tunicamycin** treatment. After 18 h of **tunicamycin** treatment, a significant inhibition of the incorporation of 3H-mannose and 3H-**glucosamine**, but slight inhibition of the incorporation of 3H-leucine into cell was obsd. The

inhibition was dose dependent. Treatment with 0.1 ug/mL **tunicamycin** for 18 h, the binding capacity of insulin to its receptor of the cell surface was decreased and the competitive binding curve pf the treated cells and the control was nearly parallel to each other. This is mainly due to the inhibition of glycosylation of newly synthesized insulin receptor by **tunicamcin**. The mechanism that deglycosylation decreased the binding capacity of insulin receptor was discussed.

ST **tunicamycin hepatocarcinoma** insulin receptor glycosylation inhibition

IT Glycosidation
(of insulin receptor, **tunicamycin** inhibition of, in human **hepatocarcinoma**)

IT **Neoplasm inhibitors**
(**hepatoma**, **tunicamycin** as, binding of insulin receptor in, of humans)

IT Liver, **neoplasm**
(**hepatoma**, inhibitors, **tunicamycin** as, binding of insulin receptor in, of humans)

IT Receptors
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin, glycosylation of, **tunicamycin** inhibition of, in human **hepatocarcinoma**)

IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(insulin receptor glycosylation inhibition by, in human **hepatocarcinoma**)

IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(insulin receptor glycosylation inhibition by, in human **hepatocarcinoma**)

RN 11089-65-9 HCAPLUS

CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2003 ACS

AN 1990:584352 HCAPLUS

DN 113:184352

TI Effect of **tunicamycin** on sialomucin and natural killer susceptibility of rat mammary **tumor** ascites cells

AU Bharathan, Seema; Moriarty, John; Moody, Charles E.; Sherblom, Anne P.

CS Dep. Biochem., Univ. Maine, Orono, ME, 04469, USA

SO Cancer Research (**1990**), 50(17), 5250-6
CODEN: CNREA8; ISSN: 0008-5472

DT Journal

LA English

CC **1-6** (Pharmacology)
Section cross-reference(s): 15

AB The MAT-B1 and MAT-C1 ascites sublines of the 13762 rat mammary **adenocarcinoma** contain a dominant cell surface complex consisting of two glycoproteins: ascites sialoglycoprotein (ASGP)-1, a Mr 600,000-700,000 peanut agglutinin-binding sialomucin, and ASGP-2, a Mr 120,000 concancavalin A-binding glycoprotein. Although both cell lines are resistant to lysis by natural killer cells, treatments which result in loss of cell surface ASGP-1 render the cells susceptible to natural killer cell lysis. Treatment of the ascites cells with 5 .mu.g/mL **tunicamycin** for 24 h effectively inhibits glycosylation of ASGP-2 without affecting cell viability or total protein synthesis. Under these conditions, expression of ASGP-1 is depressed by at least 50% in both cell lines, as monitored by [3H]**glucosamine** incorporation and by binding of peanut agglutinin to intact cells. The size distribution of O-linked oligosaccharides in ASGP-1 from **tunicamycin**-treated vs.

control MAT-**B1** cells is indistinguishable, as detd. by Bio-Gel P-4 chromatog. following alk.-borohydride treatment. Complex isolated from either treated or control cells bands at the same d. in a CsCl gradient contg. Triton X-100 and contains a diffuse band corresponding to ASGP-2 by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. **Tunicamycin**-treated cells, consistent with the reduced expression of ASGP-1, are significantly more susceptible to natural killer cell-mediated lysis, when compared to untreated controls. The results suggest that N-linked glycosylation is a prerequisite for sialomucin synthesis and/or complex formation. Thus, sialomucins may play a key role in protecting **tumor** cells from attack by the immune system, and thus agents which block sialomucin expression may be useful in limiting growth of **tumor** cells.

ST **tumor** sialomucin natural killer cell **tunicamycin**

IT **Neoplasm, composition**
(sialomucins expression in, natural killer cell susceptibility in relation to)

IT **Neoplasm inhibitors**
(**tunicamycin** as, sialomucin and natural killer susceptibility response in, in mammary cells)

IT Sialoglycoproteins
RL: BIOL (Biological study)
(ASGP-1 (ascites sialoglycoprotein 1), of mammary **neoplasm**, **tunicamycin** effect on, natural killer susceptibility in relation to)

IT Sialoglycoproteins
RL: BIOL (Biological study)
(ASGP-2 (ascites sialoglycoprotein 2), of mammary **neoplasm**, **tunicamycin** effect on, natural killer susceptibility in relation to)

IT Lymphocyte
(natural killer, mammary **neoplasm** susceptibility to, sialomucins in, **tunicamycin** effect on)

IT Mammary gland
(**neoplasm**, sialomucins and natural killer cell susceptibility in, **tunicamycin** effect on)

IT Mucins
RL: BIOL (Biological study)
(sialo-, of mammary **neoplasm**, **tunicamycin** effect on, natural killer susceptibility in relation to)

IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(mammary **neoplasm** sialomucin formation and natural killer susceptibility response to)

IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(mammary **neoplasm** sialomucin formation and natural killer susceptibility response to)

RN 11089-65-9 HCAPLUS

CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2003 ACS

AN 1987:188468 HCAPLUS

DN 106:188468

TI Minor modifications to the structure of **tunicamycin** lead to loss of the biological activity of the antibiotic

AU Hashim, Onn Haji; Cushley, William

CS Dep. Biochem., Univ. Glasgow, Glasgow, G12 8QQ, UK

SO Biochimica et Biophysica Acta (**1987**), 923(3), 362-70
CODEN: BBACAQ; ISSN: 0006-3002

DT Journal

LA English
CC **1-3** (Pharmacology)
Section cross-reference(s): 13
AB Minor alterations in the structure of **tunicamycin** [**11089-65-9**] were made in 3 different regions of the mol.; the resulting 3 analogs were employed to study the effects of such modifications upon the biol. activity of the antibiotic. The data indicate that any modification of structure results in loss of the ability of the antibiotic to inhibit N-glycosylation of proteins. In contrast to **tunicamycin** itself, none of the analogs had any deleterious effects upon cellular macromol. synthesis, nor upon the kinetics of export of de novo synthesized IgM or IgG mols. from treated rat **hybridoma** cells. In addn., the incorporation of tritiated sugars into acid-precipitable macromols. was not inhibited. Endoglycosidase H digestion of isolated IgG mols. further suggested that the analogs employed did not interfere with qual. glycosylation at the level of N-**acetylglucosamine** transferase [9054-49-3] (I and II) in the golgi app. The data are consistent with the interpretation that **tunicamycin** has very precise structural requirements for expression of inhibitory effects upon protein glycosylation, and that small variations of structure can lead to loss of its inhibitory effects.
ST **tunicamycin** antibiotic structure biol activity; protein glycosylation **tunicamycin** structure
IT Immunoglobulins
RL: BIOL (Biological study)
(formation and glycosylation and export of, in **hybridoma** cells, **tunicamycin** and its analogs effect on)
IT Proteins, biological studies
RL: RCT (Reactant); RACT (Reactant or reagent)
(glycosylation of, inhibition of, by **tunicamycin**, structure in relation to)
IT Deoxyribonucleic acid formation
Protein formation
Ribonucleic acid formation
(**tunicamycin** and its analogs effect on, in **hybridoma** cells)
IT **Hybridoma**
(**tunicamycin** and its analogs effects on macromol. formation and Ig formation and glycosylation and export in cells of)
IT Molecular structure-biological activity relationship
(protein glycosidation-inhibiting, of **tunicamycin**)
IT 9054-49-3
RL: BIOL (Biological study)
(I and II, glycosylation by, of proteins, **tunicamycin** and its analogs effect on)
IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(antibiotic, macromol. formation and Ig formation and glycosylation and export response to, in **hybridoma** cells, structure in relation to)
IT **11089-65-9D, Tunicamycin**, analogs
RL: BIOL (Biological study)
(macromol. formation and Ig formation and glycosylation and export response to, in **hybridoma** cells)
IT **11089-65-9, Tunicamycin**
RL: BIOL (Biological study)
(antibiotic, macromol. formation and Ig formation and glycosylation and export response to, in **hybridoma** cells, structure in relation to)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **11089-65-9D, Tunicamycin,** analogs
RL: BIOL (Biological study)
(macromol. formation and Ig formation and glycosylation and export response to, in **hybridoma** cells)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1986:508085 HCAPLUS
DN 105:108085
TI Response of **malignant** and **nonmalignant** epidermal cell lines to **tunicamycin**
AU Brysk, Miriam M.; Miller, Joanne; Chen, Shu Jen; Moller, Peter C.; Stach, Robert W.
CS Dep. Dermatol., Univ. Texas Med. Branch, Galveston, TX, USA
SO Cell & Tissue Research (**1986**), 245(1), 215-21
CODEN: CTSRCS; ISSN: 0302-766X
DT Journal
LA English
CC **1-6** (Pharmacology)
AB Exposure of fibroblasts to **tunicamycin** [**11089-65-9**] is **cytotoxic** for transformed cells, but not for nontransformed cells. In the present studies, with 2 mouse epidermal cell lines of common origin, a contrary pattern was seen: the **malignant** cells were more resistant to **tunicamycin** than their **nonmalignant** counterparts, as measured by growth and viability. With respect to the glycosylation of sugar precursors, the incorporation of mannose was more inhibited than that of **glucosamine**, while fucose was least affected. Sugar incorporation was less reduced in the **malignant** cells than in the normal cells, by a factor of 2 for fucose and more modestly for the other 2 sugars. There were no significant morphol. changes; in particular the desmosomal junctions were not affected. On polyacrylamide gels, variations in the intensity of several protein bands were seen in response to **tunicamycin**, but there was little difference between **malignant** and **nonmalignant** cells as measured by either Coomassie stains or concanavalin A autoradiog.
ST **tunicamycin** sensitivity epidermal cell **malignancy**; skin **tumor tunicamycin** sensitivity
IT Protein formation
(by epidermal cells, **tunicamycin** inhibition of, **malignant** state in relation to)
IT Glycoproteins
RL: FORM (Formation, nonpreparative)
(formation of, by epidermal cells, **tunicamycin** inhibition of, **malignant** state in relation to)
IT **Neoplasm inhibitors**
(**tunicamycin** as, **malignant** and **nonmalignant** epidermal cells differential sensitivity to)
IT Skin, **neoplasm**
(epidermis, **tunicamycin** sensitivity of, **malignant** state in relation to)
IT **11089-65-9**
RL: BIOL (Biological study)
(**malignant** and **nonmalignant** epidermal cell differential sensitivity to)
IT **11089-65-9**
RL: BIOL (Biological study)
(**malignant** and **nonmalignant** epidermal cell differential sensitivity to)
RN 11089-65-9 HCAPLUS

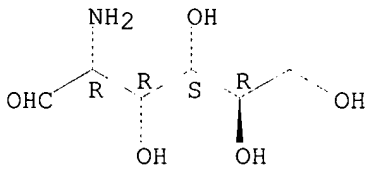
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1985:401195 HCAPLUS
DN 103:1195
TI Effects of **tunicamycin** on the expression of .beta.-adrenergic receptors in human **astrocytoma** cells during growth and recovery from agonist-induced down-regulation
AU Doss, Robert C.; Kramarcy, Neal R.; Harden, T. Kendall; Perkins, John P.
CS Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SO Molecular Pharmacology (**1985**), 27(5), 507-16
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
CC 2-8 (Mammalian Hormones)
Section cross-reference(s): **1**
AB **Tunicamycin** [**11089-65-9**] which inhibits formation of asparagine-linked glycoproteins, caused a concn.-dependent blockade of .beta.-adrenergic receptor (.beta.-AR) accumulation in 1321N1 human **astrocytoma** cells during growth in culture. A concn. of **tunicamycin** (0.1 .mu.g/mL) that inhibited receptor accumulation and 3H-labeled mannose [3458-28-4] or 3H-labeled **glucosamine** [**3416-24-8**] incorporation into glycoproteins by 90% had only a small effect (10%) on 3H-labeled leucine [61-90-5] incorporation into protein, and reduced the rate of cell growth. Incubation in drug-free medium subsequent to treatment of 1321N1 cells with **tunicamycin** for 48 h resulted in recovery of .beta.-AR to control levels within an addnl. 48 h. Exposure of cultures to (.+-.)-isoproterenol [149-53-1] (0.1 .mu.M, 12 h) caused an 80-90% loss of .beta.-AR in both pre- and postconfluent cultures; .beta.-AR recovered to control levels upon removal of isoproterenol. Although both **tunicamycin** and the protein synthesis inhibitor cycloheximide blocked .beta.-AR accumulation during growth of 1321N1 cells, neither agent inhibited the appearance of .beta.-AR during recovery from the down-regulated state in preconfluent cultures. However, cycloheximide, but not **tunicamycin**, blocked recovery of .beta.-AR after isoproterenol-induced loss of receptors in postconfluent cultures. The results with **tunicamycin** are consistent with the idea that recovery of .beta.-AR in postconfluent cultures requires the synthesis of new .beta.-AR mols., but as aglycoproteins that exhibit radioligand-binding characteristics similar to those of native glycoprotein .beta.-AR.
ST **tunicamycin** adrenoceptor **astrocytoma** expression downregulation; isoproterenol adrenoceptor downregulation **tunicamycin**; glycoprotein adrenoceptor expression downregulation **astrocytoma**
IT Glycosidation
(by **astrocytoma**, of human in culture, **tunicamycin** effect on)
IT Protein formation
(by **astrocytoma**, of human in culture, **tunicamycin** effect on .beta.-adrenergic receptor expression and down-regulation in relation to)
IT Animal tissue culture
(of **astrocytoma**, of human, .beta.-adrenergic receptor expression and down-regulation in, **tunicamycin** effect on)
IT Glycoproteins
RL: BIOL (Biological study)
(.beta.-adrenergic receptor expression and down-regulation in **astrocytoma** of human in culture in relation to)
IT Cell division
(mitosis, by **astrocytoma**, of human, **tunicamycin**

effect on .beta.-adrenergic receptors down-regulation in relation to)
IT Neuroglia
(**neoplasm**, **astrocytoma**, .beta.-adrenergic receptor
of, of human in culture, expression and down-regulation of,
tunicamycin effect on)
IT Receptors
RL: BIOL (Biological study)
(.beta.-adrenergic, of **astrocytoma**, of human in culture,
expression and down-regulation of, **tunicamycin** effect on)
IT 61-90-5, biological studies **3416-24-8** 3458-28-4
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(metab. of, by **astrocytoma** of human in culture,
tunicamycin effect on)
IT 149-53-1
RL: BIOL (Biological study)
(.beta.-adrenergic receptor down-regulation by, in **astrocytoma**
of human in culture, **tunicamycin** effect on)
IT **11089-65-9**
RL: BIOL (Biological study)
(.beta.-adrenergic receptor expression and down-regulation response to,
in **astrocytoma** of human in culture)
IT **3416-24-8**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(metab. of, by **astrocytoma** of human in culture,
tunicamycin effect on)
RN 3416-24-8 HCAPLUS
CN D-Glucose, 2-amino-2-deoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **11089-65-9**
RL: BIOL (Biological study)
(.beta.-adrenergic receptor expression and down-regulation response to,
in **astrocytoma** of human in culture)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1985:106077 HCAPLUS
DN 102:106077
TI Effects of cycloheximide and **tunicamycin** on opiate receptor
activities in **neuroblastoma** .times. **glioma** NG108-15
hybrid cells
AU Law, Ping Yee; Ungar, Harold G.; Hom, Dennis S.; Loh, Horace H.
CS Dep. Pharmacol., Univ. California, San Francisco, CA, 94143, USA
SO Biochemical Pharmacology (**1985**), 34(1), 9-17
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
CC **1-11** (Pharmacology)
AB The mol. mechanism of opiate receptor down-regulation and desensitization

was investigated by studying the effects of cycloheximide [66-81-9] and **tunicamycin** [**11089-65-9**] on opiate receptor activities in **neuroblastoma** X **glioma** NG108-15 hybrid cells. Cycloheximide inhibited [35S]-methionine and [3H]-**glucosamine** incorporation by hybrid cells, while **tunicamycin** inhibited [3H]diprenorphine binding dependents on both time and concns. of inhibitors, with no measurable modification in the ability of etorphine to regulate intracellular cyclic AMP prodn. Cycloheximide attenuated [3H]-diprenorphine binding by decreasing both the no. of sites, Bmax, and the affinity of the receptor, Kd. **Tunicamycin** treatment produced a decrease in Bmax with no apparent alteration in Kd values. Cycloheximide and **tunicamycin** did not potentiate the rate or magnitude of etorphine-induced down-regulation or desensitization of opiate receptor in NG108-15 cells. Furthermore, there was an apparent antagonism in cycloheximide action on receptor down-regulation. The reappearance of opiate binding sites after agonist removal was affected by these 2 inhibitors. Cycloheximide and **tunicamycin** eliminated the increase in [3H]-diprenorphine binding in the chronic etorphine-treated cells after agonist removal. These 2 inhibitors did not alter the resensitization of hybrid cells to etorphine. Thus, the site of opiate agonist action to induce receptor down-regulation and desensitization is not at the site of protein synthesis or protein glycosylation. These data substantiate previously reported observations that receptor down-regulation and receptor desensitization are two different cellular adaptation processes.

ST opiate receptor characterization; **neuroblastoma glioma** receptor cycloheximide **tunicamycin**

IT Receptors
RL: BIOL (Biological study)
(opiate, of **neuroblastoma-glioma** hybrid cells, cycloheximide and **tunicamycin** effect on)

IT Opiates and Opioids
RL: BIOL (Biological study)
(receptors for, in **neuroblastoma-glioma** hybrid cells, cycloheximide and **tunicamycin** effect on)

IT Neuroglia
(**neoplasm**, hybrid with **neuroblastoma**, opiate receptors of, cycloheximide and **tunicamycin** effect on)

IT Nerve, **neoplasm**
(**neuroblastoma**, hybrid with **glioma**, opiate receptors of, cycloheximide and **tunicamycin** effect on)

IT 66-81-9 **11089-65-9**
RL: BIOL (Biological study)
(opiate receptor activities in **neuroblastoma-glioma** hybrid cells in response to)

IT **11089-65-9**
RL: BIOL (Biological study)
(opiate receptor activities in **neuroblastoma-glioma** hybrid cells in response to)

RN 11089-65-9 HCAPLUS

CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2003 ACS

AN 1983:119240 HCAPLUS

DN 98:119240

TI The biochemical and ultrastructural effects of **tunicamycin** and D-**glucosamine** in L1210 leukemic cells

AU Morin, Michael J.; Porter, Carl W.; McKernan, Patricia; Bernacki, Ralph J.

CS Grace Cancer Drug Cent., New York State Dep. Health, Buffalo, NY, 14263, USA

SO Journal of Cellular Physiology (**1983**), 114(2), 162-72

CODEN: JCLLAX; ISSN: 0021-9541
DT Journal
LA English
CC **1-5** (Pharmacology)
Section cross-reference(s): 14

AB **tunicamycin** [**11089-65-9**] Was found to specifically inhibit the incorporation of a no. of sugars into L1210 leukemia cell glycoproteins. This inhibition of glycoprotein biosynthesis led to a cessation of cell growth which was reversible in a dose-dependent and time-dependent manner. After removal of the antibiotic from L1210 cell cultures, resumption of sugar incorporation preceded that of thymidine incorporation and the recovery of cell growth. The treatment of cells with **tunicamycin** resulted in a significant increase in the intracellular pool of UDP-N-**acetylglucosamine** which occurred concurrently with alterations in cell ultrastructure including distentions of the endoplasmic reticulum and nuclear membranes. Similar ultrastructural changes and increases in the intracellular pools of UDP-sugars were obsd. in L1210 cells exposeed to 5 mM D-**glucosamine** [**3416-24-8**] which suggested that the antiproliferative effects of **tunicamycin** may be related to the accumulation in the endoplasmic reticulum of 1 or more nucleotide sugar precursors of asparagine-linked glycoprotein biosynthesis. However, the biol. effects of **tunicamycin** could be distinguished from those caused by D-**glucosamine**. Exposure of L1210 cells to **tunicamycin** resulted in specific alterations in the biochem. compn. of the plasma membrane and in the inhibition of cellular agglutination by wheat germ agglutinin which were not apparent following exposure to equitoxic concns. of the aminosugar. These studies, together with those which demonstrated that recovery of the cellular capacity to synthesize glycoproteins was obligatory for the recovery of cellular proliferation in **tunicamycin**-treated cells, suggested that inhibition of the synthesis of glycoproteins was the major factor limiting L1210 leukemic **cell proliferation**.

ST **tunicamycin glucosamine** leukemia

IT Glycoproteins
RL: FORM (Formation, nonpreparative)
(formation of, leukemia cell response to **tunicamycin** in relation to)

IT **Neoplasm inhibitors**
(leukemia, **tunicamycin**)

IT **11089-65-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leukemia cell response to, **cytotoxicity** mechanism in relation to)

IT **3416-24-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leukemia cell response to, **tunicamycin cytotoxicity** in relation to)

IT **11089-65-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leukemia cell response to, **cytotoxicity** mechanism in relation to)

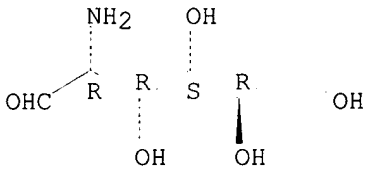
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

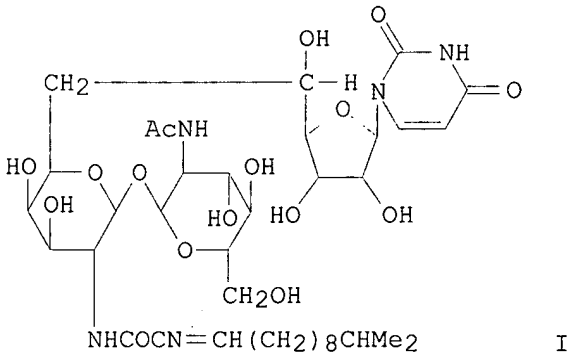
IT **3416-24-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(leukemia cell response to, **tunicamycin cytotoxicity**

in relation to)
RN 3416-24-8 HCAPLUS
CN D-Glucose, 2-amino-2-deoxy- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L125 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1983:100866 HCAPLUS
DN 98:100866
TI Selective **cytotoxicity** of purified homologs of **tunicamycin** on transformed BALB/3T3 fibroblasts
AU Seiberg, Miri; Duksin, Dan
CS Dep. Biophys., Weizmann Inst. Sci., Rehovot, 76100, Israel
SO Cancer Research (**1983**), 43(2), 845-50
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
CC **1-6** (Pharmacology)
GI



I

AB The selective **cytotoxicity** of **tunicamycin** homologs against SV40-transformed 3T3 cells (SV40-3T3) was examd. Incubation of 3T3 or virally transformed 3T3 cells with 4 different homologs (**tunicamycin A1** (I) [**66081-37-6**], **tunicamycin A2** [**76544-45-1**], **tunicamycin B1** [**66054-36-2**], and **tunicamycin B2** [**73942-09-3**] at 0.1 to 0.25 .mu.g/mL) caused detachment and death of transformed cells after 1 to 3 days, while the nontransformed cells were almost unaffected. **Cytotoxicity** against nontransformed cells occurred only when higher doses (at least 5-fold) of **A2-**, **B1-**, and **B2-tunicamycins** were used. In contrast, these homologs inhibited proliferation of 3T3 cells, even when doses of 0.5 .mu.g/mL were used. These **cytotoxic** effects were dose dependent, and maximal **cytotoxicity** of each homolog was achieved at a different concn. in

each cell type. Apparently, **tunicamycin** homologs have selective **cytotoxicity** against transformed cells. Incorporation of [3H]mannose into acid-precipitable macromols. synthesized by transformed cells was strongly inhibited (70 to 75%) by **A1**- and **B2** **-tunicamycins** at 0.01 to 0.05 .mu.g/mL, while incorporation by 3T3 cells was not affected. At higher concns. of the above **tunicamycins** (0.5 to 1 .mu.g/mL), [3H]mannose incorporation by both 3T3 and SV40-3T3 cells was inhibited more than 95%. In contrast, the effect of these **tunicamycin** homologs on protein synthesis in 3T3 and SV40-3T3 fibroblasts was less pronounced since the incorporation of amino acids was inhibited by approx. 20%. Very little inhibition of amino acid incorporation occurred when 3T3 or SV40-3T3 cells were treated with **B2-tunicamycin**. However, **A1-** **tunicamycin** inhibited [3H]proline incorporation and slightly increased [3H]tyrosine incorporation into cell layers of 3T3 cells. Examn. of secreted proteins synthesized by these cells on Na dodecyl sulfate:polyacrylamide gel electrophoresis revealed that both 3T3 and SV40-3T3 cells treated with homologs produced partially glycosylated macromols., such as procollagen and fibronectin, and failed to convert procollagen to collagen. **Tunicamycin** homologues also inhibited the N-**acetylglucosamine**-1-phosphate transferase [**11089-65-9**] activity found in microsomes prepd. from 3T3 and virally transformed 3T3 fibroblasts. Apparently, the **cytotoxic** activity of purified homologs of **tunicamycin** against transformed fibroblasts might be due to the selective inhibition of glycosylation and to the differences in the membrane solubilities of the homologs.

ST **tunicamycin cytotoxicity** transformed cell; protein glycosylation **tunicamycin cytotoxicity**

IT Proteins
RL: RCT (Reactant); RACT (Reactant or reagent)
(glycosylation of, **tunicamycin** homologs inhibition of, **cytotoxicity** to transformed cells in relation to)

IT Protein formation
(inhibition of, by **tunicamycin** homologs, **cytotoxicity** against transformed cell in relation to)

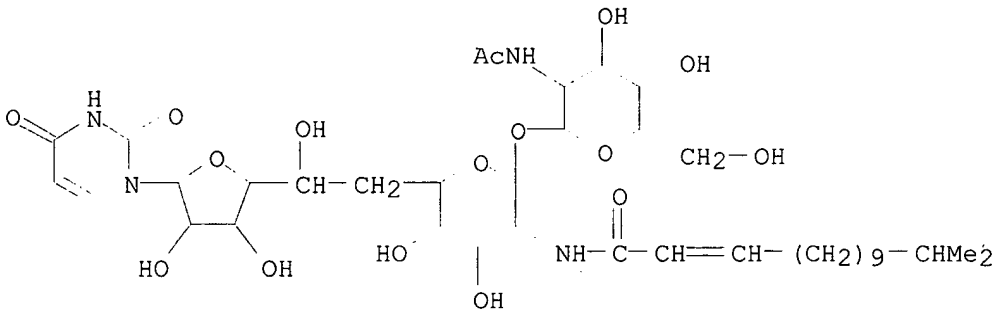
IT **Neoplasm inhibitors**
(**tunicamycin** homologs, protein formation and glycosylation inhibition in relation to)

IT **11089-65-9 66054-36-2 66081-37-6** **73942-09-3 76544-45-1**
RL: PRP (Properties)
(**cytotoxicity** of, against transformed cells, protein formation and glycosylation inhibition in relation to)

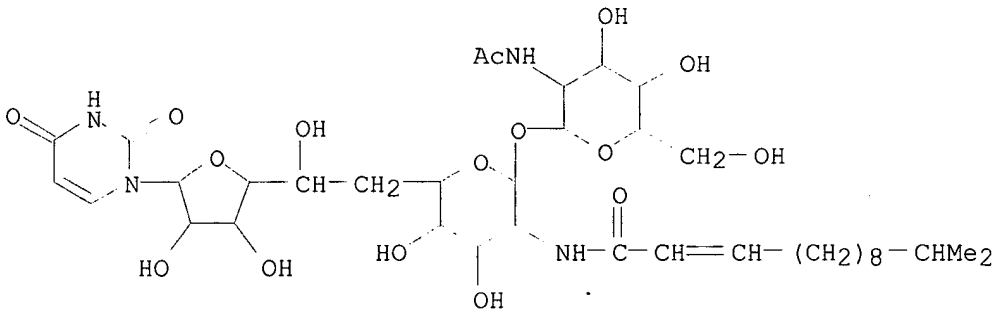
IT **11089-65-9 66054-36-2 66081-37-6** **73942-09-3 76544-45-1**
RL: PRP (Properties)
(**cytotoxicity** of, against transformed cells, protein formation and glycosylation inhibition in relation to)

RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

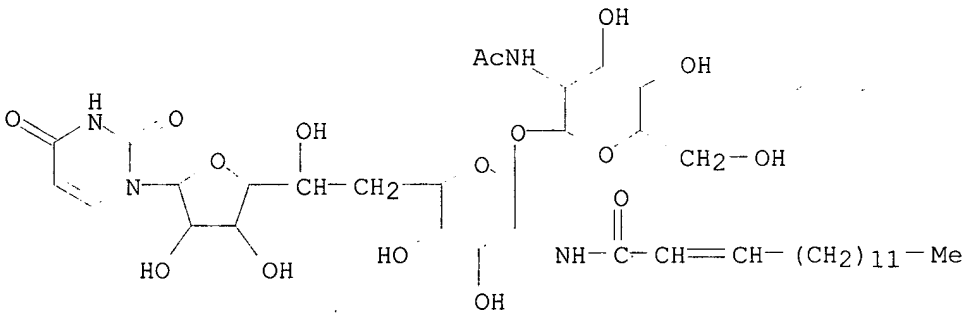
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 66054-36-2 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-13-methyl-1-oxo-2-tetradecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)



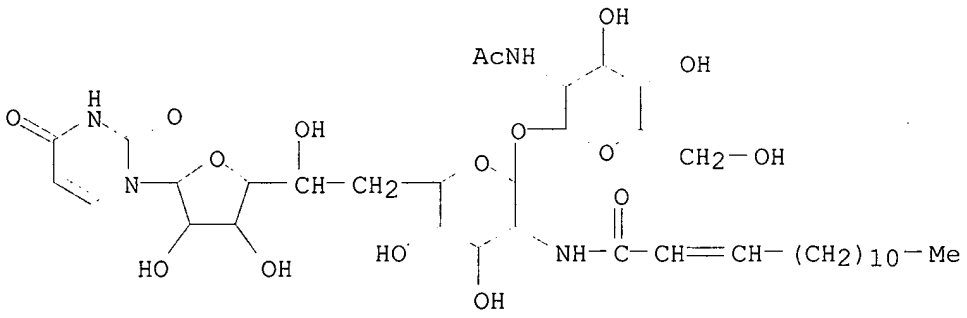
RN 66081-37-6 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-12-methyl-1-oxo-2-tridecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)



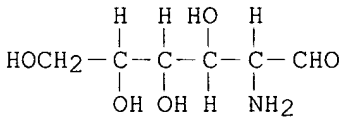
RN 73942-09-3 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-1-oxo-2-pentadecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)



RN 76544-45-1 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(11S)-11-O-[2-(acetylamino)-2-deoxy-.alpha.-D-glucopyranosyl]-6,10-dideoxy-10-[[(2E)-1-oxo-2-tetradecenyl]amino]-L-galacto-.beta.-D-allo-undecodialdo-1,4-furanose-11,7-pyranos-1-yl]- (9CI) (CA INDEX NAME)



L125 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1982:210548 HCAPLUS
DN 96:210548
TI Loss of melanogenic properties in tyrosinases induced by glycosylation inhibitors within **malignant melanoma** cells
AU Imokawa, Genji; Mishima, Yutaka
CS Sch. Med., Kobe Univ., Kobe, 650, Japan
SO Cancer Research (**1982**), 42(5), 1994-2002
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
CC **1-6** (Pharmacology)
Section cross-reference(s): 14
GI

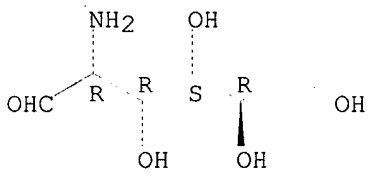


I

AB The glycosylation inhibitors, **glucosamine** (I) [**3416-24-8**] or **tunicamycin** [**11089-65-9**], have been found to be specific inhibitory modulators for melanogenesis, which is accentuated generally in **malignant melanoma** cells. Exposure to **glucosamine** (1 mg/mL) or **tunicamycin** (0.2 to 0.4 .mu.g/mL) induces a marked pigment loss within **melanoma** cells in vitro with a decrease in their growth curves. This melanogenic inhibition occurs without a substantial decrease in the synthesis of DNA, RNA, and protein in comparison with a specific, marked suppression of carbohydrate synthesis as revealed by suppressed mannose incorporation into these cells. Assay of tyrosinase [9002-10-2] of **glucosamine** - or **tunicamycin**-induced unpigmented **melanoma** cells has revealed a selective and marked decrease in the melanosome-rich large-granule fraction, but no substantial decrease in the total activity of remaining subcellular fractions. Electrophoresis of tyrosinase in the 30,000 .times. g supernatant fraction demonstrates an increase in the T1 form of sol. tyrosinase, while a disappearance of or marked decrease in membrane-bound tyrosinase, T3, is seen in the small- and large-granule fractions. Glycoprotein synthesis in the melanogenic subcellular compartments of pigment cells seems to play an integral role in melanogenesis which is principally enhanced in their **carcinogenic** status.
ST **glucosamine tunicamycin melanoma** tyrosinase melanogenesis
IT Carbohydrates and Sugars, biological studies

RL: FORM (Formation, nonpreparative)
(formation of, by **melanoma, glucosamine** and **tunicamycin** effect on, melanogenesis in relation to)
IT Glycoproteins
RL: FORM (Formation, nonpreparative)
(formation of, by **melanoma, glucosamine** and **tunicamycin** effect on, melanogenesis inhibition in relation to)
IT Melanins
RL: FORM (Formation, nonpreparative)
(formation of, **glucosamine** and **tunicamycin** inhibition of, in **melanoma**)
IT **Neoplasm inhibitors**
(**melanoma, glucosamine** and **tunicamycin** as, melanin formation inhibition in relation to)
IT **3416-24-8 11089-65-9**
RL: BIOL (Biological study)
(melanin formation response to, in **melanoma**)
IT 9002-10-2
RL: BIOL (Biological study)
(of **melanoma, glucosamine** and **tunicamycin** effect on, melanin formation in relation to)
IT **3416-24-8 11089-65-9**
RL: BIOL (Biological study)
(melanin formation response to, in **melanoma**)
RN 3416-24-8 HCAPLUS
CN D-Glucose, 2-amino-2-deoxy- (8CI, 9CI) (CA INDEX NAME)

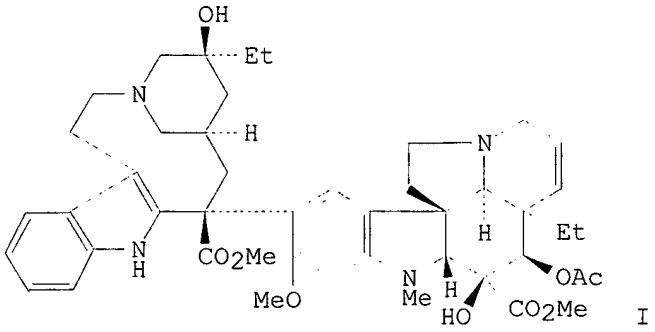
Absolute stereochemistry. Rotation (+).



RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1982:97285 HCAPLUS
DN 96:97285
TI Continued expression of vinca alkaloid resistance by CCRF-CEM cells after treatment with **tunicamycin** or pronase
AU Beck, William T.; Cirtain, Margaret C.
CS Div. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, 38101, USA
SO Cancer Research (**1982**), 42(1), 184-9
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
CC **1-6** (Pharmacology)
GI



I

AB A glycoprotein(s) with a mol. wt. of .apprx.180,000 exists on the surface of cultured leukemic lymphoblasts selected for resistance to vinblastine (VLB)(I) [865-21-4] (CEM/VLB100). The amt. of this glycoprotein, which is barely detectable on VLB-sensitive cells (CEM), appears to be related in part to the degree of resistance, up to .apprx.270-fold. Exposure of cells to pronase for 45-60 min or growth of the cells for 2 days in **tunicamycin**, an inhibitor of glycoprotein synthesis, resulted in the absence of the resistance-assocd. glycoproteins, as detd. by polyacrylamide gel electrophoresis of these treated cells after labeling the cells either with Na [3H]borohydride or with [14C]- or [3H] **glucosamine**. Uptake studies with [3H]VLB revealed that CEM cells normally accumulated and retained more drug than did the CEM/VLB100 cells. While the **tunicamycin** or pronase treatments slightly increased the uptake of drug by CEM cells, there was no enhanced uptake of [3H]VLB by the **tunicamycin**- or pronase-treated CEM/VLB100 cells, when compared with untreated controls, indicating that the loss of external surface glycoproteins did not render the resistant cells more leaky to drug influx. Addnl., diminished drug retention by the CEM/VLB100 cells was unaffected by these treatments. Moreover, when CEM/VLB100 cells were grown for 2 days in the presence of **tunicamycin** and several concns. of VLB, no enhanced toxicity of VLB was noted. Treatment with **tunicamycin** did not affect the distribution of proteins in these cells. Apparently, the carbohydrate moiety of the cell surface resistance-assocd. glycoproteins does not mediate resistance to the alkaloid per se; however, a role for plasma membrane proteins cannot be ruled out.

ST vinblastine resistance leukemia glycoprotein membrane

IT Cell membrane
(glycoprotein of, of leukemic lymphoblast, vinblastine resistance in relation to)

IT Glycoproteins
RL: BIOL (Biological study)
(of leukemic lymphoblast cell membrane, vinblastine resistance in relation to)

IT Drug resistance
(to vinblastine, of leukemic lymphoblast, glycoprotein of cell membrane role in)

IT **Neoplasm inhibitors**
(leukemia, vinblastine as, resistance to, glycoprotein of lymphoblast cell membrane role in)

IT 865-21-4
RL: BIOL (Biological study)
(resistance to, of leukemic lymphoblast, glycoprotein of cell membrane role in)

L125 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1980:140464 HCAPLUS

DN 92:140464
TI Induction of differentiation of human and murine myeloid leukemia cells in culture by **tunicamycin**
AU Nakayasu, Michie; Terada, Masaaki; Tamura, Gakuzo; Sugimura, Takashi
CS Natl. Cancer Cent. Res. Inst., Tokyo, 104, Japan
SO Proceedings of the National Academy of Sciences of the United States of America (**1980**), 77(1), 409-13
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC **1-4** (Pharmacodynamics)
Section cross-reference(s): 14
AB **Tunicamycin** [**11089-65-9**], an antibiotic that specifically blocks the synthesis of N-**acetylglucosamine**-lipid intermediates and thereby prevents glycosylation of glycoproteins, induced differentiation of both human (HL-60) and murine (M1) myeloid leukemia cell l. At 0.1-1.0 .mu.g/mL, it induced differentiation of both HL-60 and M1 cells, characterized by an increase in phagocytic cells and changes to resemble mature myeloid cells. Fc receptors were also induced in M1 but not in HL-60 cells; induction of intracellular lysozyme activity was not detected in either HL-60 or M1 cells. With this concn. of **tunicamycin**, there was marked decrease in rate of incorporation of radioactive **glucosamine** into macromols. and a decrease in the rate of DNA synthesis. These data show that glycosylation of cellular proteins has an important role in maintaining these myeloid leukemia cells in an undifferentiated state in culture. The results also indicate that induction of phagocytosis in both HL-60 and M1 myeloid leukemia cells and of Fc receptors in M1 cells does not require continued synthesis of the oligosaccharide portions of cellular proteins by the lipid-linked pathway.
ST myeloid leukemia differentiation **tunicamycin**
IT **Leukemia**
(myeloid, differentiation of, **tunicamycin** induction of)
IT **11089-65-9**
RL: BIOL (Biological study)
(myeloid leukemia cells differentiation induction by)
IT **11089-65-9**
RL: BIOL (Biological study)
(myeloid leukemia cells differentiation induction by)
RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L125 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS
AN 1979:1078 HCAPLUS
DN 90:1078
TI Effect of **tunicamycin** on IgM, IgA, and IgG secretion by mouse **plasmacytoma** cells
AU Hickman, Scot; Kornfeld, Stuart
CS Dep. Med. Biochem., Washington Univ. Sch. Med., St. Louis, MO, USA
SO Journal of Immunology (**1978**), 121(3), 990-6
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
CC 3-5 (Biochemical Interactions)
Section cross-reference(s): **1**, 15
AB **Tunicamycin** [**11089-65-9**], an antibiotic that prevents glycosylation of glycoproteins by blocking the formation of N-**acetylglucosamine**-lipid intermediates, was used to study the importance of glycosylation for the secretion of Igs by mouse **plasmacytoma** lines that produce Igs of different classes. **Tunicamycin**, at 0.5 .mu.g/mL produced an 81% inhibition of IgM secretion by MOPC 104E plasma cells without significantly affecting the

initial rate of synthesis of intracellular IgM. No increase in the intracellular degrdn. of nonglycosylated IgM could be demonstrated. **Tunicamycin** also produced a 64% inhibition of IgA secretion by several mouse IgA-secreting **plasmacytoma** lines. In contrast, despite inhibiting the incorporation of D-**glucosamine**-14C into newly synthesized IgG, **tunicamycin** only produced a 28% inhibition of IgG secretion; this was only slightly more than the nonspecific inhibition of secretion of the normally nonglycosylated .lambda.2 light chains by variant MOPC 315 **plasmacytomas**. Therefore, the extent of inhibition of Ig secretion produced by **tunicamycin** depends on the Ig class produced by the plasma cell.

ST Ig release **plasmacytoma tunicamycin**; glycoprotein formation **plasmacytoma tunicamycin**

IT Immunoglobulins
RL: BIOL (Biological study)
(A, secretion of, by **plasmacytoma** cells, **tunicamycin** effect on)

IT Immunoglobulins
RL: BIOL (Biological study)
(G, secretion of, by **plasmacytoma** cells, **tunicamycin** effect on)

IT Immunoglobulins
RL: BIOL (Biological study)
(M, secretion of, by **plasmacytoma** cells, **tunicamycin** effect on)

IT **Myeloma**
(**plasma-cell**, Igs secretion by, **tunicamycin** effect on)

IT **11089-65-9**
RL: PRP (Properties)
(Igs formation inhibition by, in **plasmacytoma** cells)

IT **11089-65-9**
RL: PRP (Properties)
(Igs formation inhibition by, in **plasmacytoma** cells)

RN 11089-65-9 HCAPLUS
CN Tunicamycin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> fil medline
FILE 'MEDLINE' ENTERED AT 15:01:02 ON 08 APR 2003

FILE LAST UPDATED: 6 APR 2003 (20030406/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L164 ANSWER 1 OF 13 MEDLINE
AN 2001067546 MEDLINE
DN 20536356 PubMed ID: 11082285
TI Myoepithelial-specific CD44 shedding contributes to the anti-invasive and **antiangiogenic** phenotype of myoepithelial cells.
AU Alpaugh M L; Lee M C; Nguyen M; Deato M; Dishakjian L; Barsky S H
CS Department of Pathology, UCLA School of Medicine, Los Angeles, California

90024, USA.
NC CA 71195 (NCI)
CA 83111 (NCI)
SO EXPERIMENTAL CELL RESEARCH, **(2000 Nov 25)** 261 (1) 150-8.
Journal code: 0373226. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222
AB Myoepithelial cells surround incipient ductal carcinomas of the breast and exert anti-invasive and **antiangiogenic** effects in vitro through the elaboration of suppressor molecules. This study examines one putative molecule, solubilized CD44 produced by myoepithelial shedding of membrane CD44. Studies with different human myoepithelial cell lines demonstrate that myoepithelial cells express and shed both the 85-kDa standard (CD44s) and the 130-kDa epithelial (CD44v8-10) isoforms, findings further confirmed by the use of isoform-specific antibodies. PMA pretreatment enhances CD44 shedding detected by two different methods at different time points: a reduction in surface CD44 at 2 h by flow cytometry and a marked decrease in both total cellular CD44 and plasma membrane CD44 at 12 h by Western blot. This shedding is both specific for CD44 and specific for myoepithelial cells. This shedding is inhibited by the chymotrypsin inhibitors chymostatin and alpha(1)-antichymotrypsin but not by general metallo-, cysteine, or other serine proteinase inhibitors. Myoepithelial-cell-conditioned medium and affinity-purified solubilized CD44 from this conditioned medium block hyaluronan adhesion and migration of both human carcinoma cell lines and human umbilical vein endothelial cells.

CT Check Tags: Female; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Antigens, CD: PH, physiology
Antigens, CD44: DE, drug effects
*Antigens, CD44: PH, physiology
Breast Neoplasms
Carcinoma
Culture Media, Conditioned
Epithelial Cells: CY, cytology
Epithelial Cells: PH, physiology
***Neoplasm Invasiveness: PC, prevention & control**
***Neovascularization, Pathologic: PC, prevention & control**
Protease Inhibitors: PD, pharmacology
Protein Isoforms: PH, physiology
Tetradecanoylphorbol Acetate: PD, pharmacology
Tissue-Inhibitor of Metalloproteinase-1: PD, pharmacology
Tumor Cells, Cultured
Tunicamycin: PD, pharmacology
RN **11089-65-9 (Tunicamycin)**; 16561-29-8 (Tetradecanoylphorbol Acetate)
CN 0 (Antigens, CD); 0 (Antigens, CD44); 0 (Culture Media, Conditioned); 0 (Protease Inhibitors); 0 (Protein Isoforms); 0 (Tissue-Inhibitor of Metalloproteinase-1)

L164 ANSWER 2 OF 13 MEDLINE
AN 2001054584 MEDLINE
DN 20406214 PubMed ID: 10949666
TI **Tunicamycin** inhibits capillary endothelial cell proliferation by inducing apoptosis. Targeting dolichol-pathway for generation of new anti-**angiogenic** therapeutics.

AU **Martinez J A**; Torres-Negron I; Amigo L A; Roldan R A; Mendez A; **Banerjee D K**
CS Department of Biochemistry, School of Medicine, University of Puerto Rico, San Juan 00936-5067, USA.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, **(2000)** 476 197-208. Ref: 29
Journal code: 0121103. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200012
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001214
AB Bovine adrenal medulla microvascular endothelial cells used in this study undergo cellular proliferation and differentiation upon culturing in vitro as observed both by light and scanning electron microscopy. Cells also respond to the growth promoting activity of serum and basic fibroblast growth factor (FGF2). Flow cytometric analysis of a synchronized culture established that cells take 68 hours to complete one cell cycle spending 36 hours in the G1 phase, 8 hours in the S phase, and 24 hours in the G2 + M phase when cultured in EMEM containing 2% heat-inactivated fetal bovine serum (FBS). At 10% serum, or in the presence of FGF2 (10 ng/ml-100 ng/ml) length of the cell cycle is reduced to 56 hours due to shortening of the G1 phase by 12 hours. **Tunicamycin** (a glucosamine-containing pyrimidine nucleotide), and an inhibitor of glucosaminyl-1-phosphate (GlcNAc 1-P) transferase, the first step of Glc3Man9GlcNAc2-PP-Dol (OSL) biosynthesis is found to inhibit the endothelial cells proliferation by inducing apoptosis as observed by flow cytometry and DNA laddering. Cell shrinkage, compaction of nuclei, membrane fragmentation, etc., typical of apoptotic response are frequently seen by light microscopy in the presence of **tunicamycin**. Scanning electron microscopy also exhibited a considerable amount of cell surface blebbing. Accumulation of an immunopositive cell specific asparagine-linked (N-linked) glycoprotein, Factor VIII:C in the absence of Glc3Man9GlcNAc2-PP-Dol in **tunicamycin** treated cells has been proposed as an apoptotic triggering mechanism under the current experimental conditions.
CT Check Tags: Animal; Support, Non-U.S. Gov't
*Apoptosis: DE, drug effects
Asparagine: ME, metabolism
Capillaries: CY, cytology
Cattle
Cell Division: DE, drug effects
Cells, Cultured
Clone Cells
*Endothelium, Vascular: CY, cytology
Factor VIII: ME, metabolism
Glycoproteins: ME, metabolism
*Mannosyltransferases: ME, metabolism
*Neovascularization, Pathologic: ME, metabolism
*Polyisoprenyl Phosphate Sugars: BI, biosynthesis
Tunicamycin: ME, metabolism
***Tunicamycin: PD, pharmacology**
RN **11089-65-9 (Tunicamycin)**; 7006-34-0 (Asparagine); 9001-27-8 (Factor VIII)
CN 0 (Glc(3)Man(9)(GlcNAc)(2)-diphosphate-dolichol); 0 (Glycoproteins); 0 (Polyisoprenyl Phosphate Sugars); EC 2.4.1. (Mannosyltransferases); EC 2.4.1.83 (GDPmannose dolicholphosphate mannosyltransferase)

L164 ANSWER 3 OF 13 MEDLINE

AN 2000394502 MEDLINE
DN 20359918 PubMed ID: 10775505
TI Normal human fibroblasts produce membrane-bound and soluble isoforms of FGFR-1.
AU Root L L; Shipley G D
CS Legacy Clinical Research and Technology Center, Portland, Oregon, 97208-3950, USA.. lroot@lhs.org
SO MOLECULAR CELL BIOLOGY RESEARCH COMMUNICATIONS, **(2000 Feb)** 3 (2) 87-97.
Journal code: 100889076. ISSN: 1522-4724.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000815
AB Fibroblast growth factors (FGFs) are polypeptide mitogens for a wide variety of cell types and are involved in other processes such as **angiogenesis** and cell differentiation. FGFs mediate their biological responses by activating high-affinity tyrosine kinase receptors. Currently, there are four human fibroblast growth factor receptor (FGFR) genes. To investigate the mechanisms by which alpha FGF and beta FGF may mediate mitogenic signal transduction in human skin-derived fibroblasts, we analyzed these cells for the presence of high-affinity FGFRs. We show that normal human dermal fibroblasts express a single high-affinity FGFR gene, FGFR-1. Cloning and sequencing of two distinct FGFR-1 cDNAs suggested that normal human dermal fibroblasts express a membrane-bound and a putatively secreted form of FGFR-1. We show that normal human dermal fibroblasts produce two FGFR-1 proteins, one of which exists in conditioned media. The mRNA for the putatively secreted form of FGFR-1 appears to be down-regulated by serum treatment of the cells.

CT Check Tags: Human
Base Sequence
Blood
Cells, Cultured
Culture Media, Conditioned
DNA Primers
Down-Regulation
Fibroblasts: DE, drug effects
Fibroblasts: ME, metabolism
*Protein Isoforms: BI, biosynthesis
Protein Isoforms: GE, genetics
Protein Isoforms: ME, metabolism
*Receptor Protein-Tyrosine Kinases: BI, biosynthesis
Receptor Protein-Tyrosine Kinases: GE, genetics
Receptor Protein-Tyrosine Kinases: ME, metabolism
*Receptors, Fibroblast Growth Factor: BI, biosynthesis
Receptors, Fibroblast Growth Factor: GE, genetics
Receptors, Fibroblast Growth Factor: ME, metabolism
Solubility
Translation, Genetic
Tunicamycin: PD, pharmacology
RN **11089-65-9 (Tunicamycin)**
CN 0 (Culture Media, Conditioned); 0 (DNA Primers); 0 (Protein Isoforms); 0 (Receptors, Fibroblast Growth Factor); 0 (fibroblast growth factor receptor 1); EC 2.7.11.- (Receptor Protein-Tyrosine Kinases)

L164 ANSWER 4 OF 13 MEDLINE
AN 1999199620 MEDLINE

DN 99199620 PubMed ID: 10099847
TI Expression of Glc3Man9GlcNAc2-PP-Dol is a prerequisite for capillary endothelial cell proliferation.
AU **Martinez J A**; Torres-Negron I; Amigo L A; **Banerjee D K**
CS Department of Biochemistry, School of Medicine, University of Puerto Rico, San Juan 00936-5067, USA.
SO CELLULAR AND MOLECULAR BIOLOGY, **(1999 Feb)** 45 (1) 137-52.
Journal code: 9216789. ISSN: 0145-5680.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990719
AB Protein N-glycosylation has been proposed to be intimately involved in the migration, proliferation and differentiation of endothelial cells. Using a synchronized, non-transformed capillary endothelial cell line from bovine adrenal medulla as a model, and the N-glycosylation inhibitor, **tunicamycin**, we have elucidated the molecular basis of the dolichol pathway in the **angiogenic** process. The synchronized culture required approximately 68 hrs. to complete one cell cycle, cells spending nearly 36 hrs. in G1 phase, 8 hrs. in S phase and 24 hrs. in G2 + M phase when maintained in 2% fetal bovine serum (heat-inactivated). The cell cycle however, was shortened due to a reduction of the G1 phase by 12-16 hrs. when the serum concentration was increased to 10%, or when beta FGF (1 or 10 nanogram) was added into the culture media containing 2% serum. Light microscopy and scanning electron microscopy both supported these proliferative responses. Serum concentration below 2% arrested cell proliferation and induced capillary lumen-like structure formation with 48 hrs. Expression of the blood clotting antigen factor VIII:C (a M(r) 270,000 dalton N-linked glycoprotein and a marker of our endothelial cells) preceded the endothelial cell proliferation and established a temporal relationship. **Tunicamycin**, an inhibitor of Glc3Man9GlcNAc2-PP-Dol biosynthesis, a prerequisite for N-linked protein glycosylation in the ER-inhibited the cell growth and proliferation in a time and dose-dependent manner with a concomitant accumulation of immunopositive, non-glycosylated factor VIII:C in the conditioned media. **Tunicamycin** also caused surface blebbing and induction of programmed cell death (PCD)(apoptosis) within 32 hrs. Absence of cellular growth and proliferation, surface blebbing and the induction of PCD in the presence of **tunicamycin**, provided conclusive evidence that normal expression of Glc3Man9GlcNAc2-PP-Dol is an essential event for capillary proliferation during **angiogenesis**.
CT Check Tags: Support, Non-U.S. Gov't
Apoptosis
Cell Cycle
*Cell Division
Cells, Cultured
Dose-Response Relationship, Drug
*Endothelium, Vascular: PH, physiology
Enzyme-Linked Immunosorbent Assay
Factor VIII: ME, metabolism
Fibroblast Growth Factor 2: ME, metabolism
Flow Cytometry
Glycosylation
Microscopy, Electron, Scanning
*Polyisoprenyl Phosphate Sugars: PH, physiology
Time Factors
Tunicamycin: PD, pharmacology
RN **103107-01-3 (Fibroblast Growth Factor 2); 11089-65-9 (Tunicamycin)**; 9001-27-8 (Factor VIII)

CN 0 (Glc(3)Man(9)(GlcNAc)(2)-diphosphate-dolichol); 0 (Polyisoprenyl Phosphate Sugars)

L164 ANSWER 5 OF 13 MEDLINE
AN 97266064 MEDLINE
DN 97266064 PubMed ID: 9111868
TI CD44: structure, function, and association with the malignant process.
AU Naot D; Sionov R V; Ish-Shalom D
CS Lautenberg Center for General and Tumor Immunology, Hebrew University-Hadassah Medical School, Jerusalem, Israel.
SO ADVANCES IN CANCER RESEARCH, **(1997)** 71 241-319. Ref: 489
Journal code: 0370416. ISSN: 0065-230X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199706
ED Entered STN: 19970709
Last Updated on STN: 19990129
Entered Medline: 19970620
AB CD44 is a ubiquitous multistructural and multifunctional cells surface adhesion molecule involved in cell-cell and cell-matrix interactions. Twenty exons are involved in the genomic organization of this molecule. The first five and the last 5 exons are constant, whereas the 10 exons located between these regions are subjected to alternative splicing, resulting in the generation of a variable region. Differential utilization of the 10 variable region exons, as well as variations in N-glycosylation, O-glycosylation, and glycosaminoglycanation (by heparan sulfate or chondroitin sulfate), generate multiple isoforms (at least 20 are known) of different molecular sizes (85-230 kDa). The smallest CD44 molecule (85-95 kDa), which lacks the entire variable region, is standard CD44 (CD44s). As it is expressed mainly on cells of lymphohematopoietic origin, CD44s is also known as hematopoietic CD44 (CD44H). CD44s is a single-chain molecule composed of a distal extracellular domain (containing, the ligand-binding sites), a membrane-proximal region, a transmembrane-spanning domain, and a cytoplasmic tail. The molecular sequence (with the exception of the membrane-proximal region) displays high interspecies homology. After immunological activation, T lymphocytes and other leukocytes transiently upregulate CD44 isoforms expressing variant exons (designated CD44v). A CD44 isform containing the last 3 exon products of the variable region (CD44V8-10, also known as epithelial CD44 or CD44E), is preferentially expressed on epithelial cells. The longest CD44 isoform expressing in tandem eight exons of the variable region (CD44V3-10) was detected in keratinocytes. Hyaluronic acid (HA), an important component of the extracellular matrix (ECM), is the principal, but by no means the only, ligand of CD44. Other CD44 ligands include the ECM components collagen, fibronectin, laminin, and chondroitin sulfate. Mucosal addressin, serglycin, osteopontin, and the class II invariant chain (Ii) are additional, ECM-unrelated, ligands of the molecule. In many, but not in all cases, CD44 does not bind HA unless it is stimulated by phorbol esters, activated by agonistic anti-CD44 antibody, or deglycosylated (e.g., by **tunicamycin**). CD44 is a multifunctional receptor involved in cell-cell and cell-ECM interactions, cell traffic, lymph node homing, presentation of chemokines and growth factors to traveling cells, and transmission of growth signals. CD44 also participates in the uptake and intracellular degradation of HA, as well as in transmission of signals mediating hematopoiesis and apoptosis. Many cancer cell types as well as their metastases express high levels of CD44. Whereas some tumors, such as gliomas, exclusively express standard CD44, other neoplasms, including gastrointestinal cancer, bladder cancer, uterine cervical cancer, breast cancer and non-Hodgkin's lymphomas, also express CD44 variants. Hence

CD44, particularly its variants, may be used as diagnostic or prognostic markers of at least some human malignant diseases. Furthermore, it has been shown in animal models that injection of reagents interfering with CD44-ligand interaction (e.g., CD44s- or CD44v-specific antibodies) inhibit local tumor growth and metastatic spread. These findings suggest that CD44 may confer a growth advantage on some neoplastic cells and, therefore, could be used as a target for cancer therapy. It is hoped that identification of CD44 variants expressed on cancer but not on normal cells will lead to the development of anti-CD44 reagents restricted to the neoplastic growth.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't
Alternative Splicing
*Antigens, CD44: PH, physiology
Apoptosis
Arthritis, Rheumatoid: PP, physiopathology
Binding Sites
Cell Adhesion
*Cell Adhesion Molecules: PH, physiology
Cell Aggregation
Cell Movement
Cytokines: ME, metabolism
Cytoskeleton: PH, physiology
Endometrium: PH, physiology
Endothelium: CY, cytology
Extracellular Matrix: ME, metabolism
Genes, Structural
Glycosylation
Growth Substances: ME, metabolism
Hematopoiesis
*Hyaluronic Acid: ME, metabolism
Ligands
Malaria: IM, immunology
Membrane Glycoproteins: PH, physiology
Menstruation
Neoplasm Metastasis
***Neoplasms: PA, pathology**
Terminology
Wound Healing

RN 9004-61-9 (Hyaluronic Acid)

CN 0 (Antigens, CD44); 0 (Cell Adhesion Molecules); 0 (Cytokines); 0 (Growth Substances); 0 (Ligands); 0 (Membrane Glycoproteins)

L164 ANSWER 6 OF 13 MEDLINE

AN 94274239 MEDLINE

DN 94274239 PubMed ID: 7516308

TI Is asparagine-linked protein glycosylation an obligatory requirement for **angiogenesis**?.

AU **Banerjee D K**; Vendrell-Ramos M

CS Department of Biochemistry, School of Medicine, University of Puerto Rico, San Juan 00936-5067.

NC SO6RR08224 (NCRR)

SO INDIAN JOURNAL OF BIOCHEMISTRY AND BIOPHYSICS, **(1993 Dec)** 30 (6) 389-94.
Journal code: 0310774. ISSN: 0301-1208.

CY India

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199407

ED Entered STN: 19940729
Last Updated on STN: 19970203
Entered Medline: 19940719

AB Dependence of protein N-glycosylation on capillary endothelial cell

proliferation has been studied. Amphomycin, a potent N-glycosylation inhibitor, inhibited capillary endothelial cell proliferation in a dose-dependent manner. beta-Agonist isoproterenol as well as other intracellular cAMP enhancing agents, viz. cholera toxin, prostaglandin E1 and 8Br-cAMP, also enhanced capillary endothelial cell proliferation. In addition to cell proliferation, isoproterenol also enhanced protein glycosylation in these cells. Isoproterenol effect was mediated by beta-adrenoreceptors, as it got reduced on pre-treatment of cells with either atenolol or ICI 118, 551 or propranolol. Furthermore, isoproterenol stimulation of protein glycosylation by exogenous dolichyl monophosphate and its inhibition by **tunicamycin** (GlcNAc-1P transferase inhibitor) supported the concept that isoproterenol specifically stimulated protein N-glycosylation event(s) in the cell.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
8-Bromo Cyclic Adenosine Monophosphate: PD, pharmacology
Adrenal Medulla: CY, cytology
Adrenal Medulla: DE, drug effects
Adrenal Medulla: ME, metabolism
Adrenergic beta-Antagonists: PD, pharmacology
Alprostadil: PD, pharmacology
Antibiotics: PD, pharmacology
*Asparagine
Cattle
Cell Division: DE, drug effects
Cells, Cultured
Cholera Toxin: PD, pharmacology
Cyclic AMP: ME, metabolism
*Endothelium, Vascular: CY, cytology
Endothelium, Vascular: DE, drug effects
*Endothelium, Vascular: ME, metabolism
Glycosylation: DE, drug effects
Isoproterenol: PD, pharmacology
*Neovascularization, Pathologic
Oligopeptides: PD, pharmacology
*Protein Processing, Post-Translational: DE, drug effects

RN 1402-82-0 (amphomycin); 23583-48-4 (8-Bromo Cyclic Adenosine Monophosphate); 60-92-4 (Cyclic AMP); 7006-34-0 (Asparagine); 745-65-3 (Alprostadil); 7683-59-2 (Isoproterenol); 9012-63-9 (Cholera Toxin)

CN 0 (Adrenergic beta-Antagonists); 0 (Antibiotics); 0 (Oligopeptides)

L164 ANSWER 7 OF 13 MEDLINE

AN 94130961 MEDLINE

DN 94130961 PubMed ID: 7507845

TI A novel soluble form of mouse VCAM-1 is generated from a glycolipid-anchored splicing variant.

AU Hahne M; Lenter M; Jager U; Vestweber D

CS Hans Spemann Laboratory, Max-Planck-Institute for Immunology, Freiburg, FRG.

SO EUROPEAN JOURNAL OF IMMUNOLOGY, **(1994 Feb)** 24 (2) 421-8.
Journal code: 1273201. ISSN: 0014-2980.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199403

ED Entered STN: 19940318
Last Updated on STN: 19960129
Entered Medline: 19940309

AB VCAM-1 is a cytokine-induced endothelial adhesion molecule which belongs to the immunoglobulin (Ig) superfamily and mediates the binding of various leukocytes. In addition to the 110-kDa form of VCAM-1, we have found four additional glycoproteins on mouse brain-derived endothelioma cells after stimulation with tumor necrosis factor-alpha (TNF-alpha), which are

recognized by several monoclonal antibodies against VCAM-1. Biochemical analysis revealed that the two smaller proteins (35 kDa and 37 kDa) are intracellular precursors of the two larger forms (44 kDa and 45 kDa), that the 44 kDa and 45 kDa proteins are glycolipid-anchored at the cell surface and that they differ in their N-glycosylation. Most likely they are identical to the recently identified glycolipid-anchored splice variant of VCAM-1, since they are recognized by the M3 antiserum which we raised against a peptide from the unique protein domain of this splicing variant. With the help of this antiserum we could show by immunohistology that the corresponding VCAM-1 protein variant is induced in vivo by lipopolysaccharide (LPS) on endothelium of the mouse. In addition, we found a 42-kDa soluble form of VCAM-1 in the serum of LPS-stimulated mice, which was recognized by the M3 antiserum. This soluble form was undetectable in the serum of unstimulated mice in contrast to the soluble 100-kDa form of VCAM-1 which was clearly detected in serum of unstimulated mice and only increased 2-3-fold upon stimulation with LPS. Thus, only the expression of the 42-kDa shredded form and not of the 100-kDa soluble form of VCAM-1 is strictly dependent on stimulation by LPS.

CT Check Tags: Animal
*Cell Adhesion Molecules: CH, chemistry
Cell Adhesion Molecules: ME, metabolism
Cell Line
Endothelium, Vascular: CH, chemistry
Endothelium, Vascular: IM, immunology
Glycoproteins: ME, metabolism
Glycosylation
Glycosylphosphatidylinositols
Hemangioendothelioma: CH, chemistry
Hemangioendothelioma: IM, immunology
Lipopolysaccharides: PD, pharmacology
Mice
Mice, Inbred C57BL
Molecular Weight
Protein Precursors: ME, metabolism
Protein Processing, Post-Translational
Solubility
Tumor Necrosis Factor: PD, pharmacology
Tunicamycin: PD, pharmacology
Vascular Cell Adhesion Molecule-1

RN **11089-65-9 (Tunicamycin)**

CN 0 (Cell Adhesion Molecules); 0 (Glycoproteins); 0 (Glycosylphosphatidylinositols); 0 (Lipopolysaccharides); 0 (Protein Precursors); 0 (Tumor Necrosis Factor); 0 (**Vascular** Cell **Adhesion** Molecule-1)

L164 ANSWER 8 OF 13 MEDLINE

AN 91060546 MEDLINE

DN 91060546 PubMed ID: 2246236

TI Characterization of the receptors for vascular endothelial growth factor.

AU Vaisman N; Gospodarowicz D; Neufeld G

CS Department of Biology, Israel Institute of Technology, Technion City, Haifa.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1990 Nov 15)** 265 (32) 19461-6. Journal code: 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199101

ED Entered STN: 19910222
Last Updated on STN: 19910222
Entered Medline: 19910108

AB Vascular endothelial growth factor (vEGF) is a recently discovered mitogen

for endothelial cells. It is also a potent **angiogenic** factor. We have characterized the vEGF receptors of endothelial cells using both binding and cross-linking techniques. Scatchard analysis of equilibrium binding experiments revealed two types of high-affinity binding sites on the cell surfaces of bovine endothelial cells. One of the sites has a dissociation constant of 10(-12) M and is present at a density of 3 x 10(3) receptors/cell. The other has a dissociation constant of 10(-11) M, with 4 x 10(4) receptors/cell. A high molecular weight complex containing 125I-vEGF is formed when 125I-vEGF is cross-linked to bovine endothelial cells. This complex has an apparent molecular mass of 225 kDa. Two other faintly labeled complexes with apparent molecular masses of 170 and 195 kDa also are detected. Reduction in the presence of dithiothreitol causes a substantial increase in the labeling intensity of the 170- and 195-kDa complexes, suggesting that these complexes are derived from the 225-kDa complex by reduction of disulfide bonds. The labeling of the vEGF receptors was inhibited by an excess of unlabeled vEGF but not by high concentrations of several other growth factors. Suramin and protamine, as well as several species of lectins, inhibited the binding. The expression of functional vEGF receptors was inhibited when the cells were preincubated with **tunicamycin**, indicating that glycosylation of the receptor is important for the expression of functional vEGF receptors. Pretreatment with swainsonine on the other hand, did not prevent formation of functional receptors. However, the mass of the 225-kDa complex is decreased by 20 kDa when 125I-vEGF is cross-linked to swainsonine-treated endothelial cells.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Cattle
Cell Line
Cross-Linking Reagents
Disulfides: ME, metabolism
Dithiothreitol: PD, pharmacology
Electrophoresis, Polyacrylamide Gel
*Endothelial Growth Factors: ME, metabolism
*Endothelium, Vascular: ME, metabolism
Glycosylation
Hamsters
Mice
Mice, Inbred BALB C
Molecular Weight
Protamines: PD, pharmacology
Receptors, Mitogen: AI, antagonists & inhibitors
*Receptors, Mitogen: ME, metabolism
Suramin: PD, pharmacology
Tunicamycin: PD, pharmacology

RN **11089-65-9 (Tunicamycin)**; 145-63-1 (Suramin); 3483-12-3 (Dithiothreitol)

CN 0 (Cross-Linking Reagents); 0 (Disulfides); 0 (Endothelial Growth Factors); 0 (Protamines); 0 (Receptors, Mitogen); 0 (endothelial growth factor receptor)

L164 ANSWER 9 OF 13 MEDLINE

AN 91009295 MEDLINE

DN 91009295 PubMed ID: 1698786

TI Production of two variant laminin forms by endothelial cells and shift of their relative levels by angiostatic steroids.

AU Tokida Y; Aratani Y; Morita A; Kitagawa Y

CS Institute for Biochemical Regulation, School of Agriculture, Nagoya University, Japan.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1990 Oct 25)** 265 (30) 18123-9. Journal code: 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199011
ED Entered STN: 19910117
Last Updated on STN: 19960129
Entered Medline: 19901115
AB Organization of endothelium as the lining of the cardiovascular system is supported by basement membrane. The important role of laminin and other basement membrane proteins is assumed in the **angiogenesis**. We show here that cultured endothelial cells produce two forms of laminin, and their relative levels are changed by **antiangiogenic** steroids. The synthesis of laminin subunits by endothelial cells isolated from bovine aorta and from bovine pulmonary artery was studied by metabolic labeling with [35S]methionine. Both endothelial cells produced a novel laminin-related polypeptide (A' subunit) in addition to the A, B1, and B2 subunits. Two-dimensional sodium dodecyl sulfate gel electrophoretic analysis showed that the B1B2 complex was first formed and the A subunit joined it to form the AB1B2 complex or the A' subunit joined it to form A'B1B2 complex. This mechanism implied that replacement of subunits in the complex by a corresponding variant produces variety in the structure and function of laminin. The A'B1B2 complex was the major product in endothelial cells under normal culture conditions. An angiostatic steroid, medroxyprogesterone, suppressed the A' synthesis and stimulated the A synthesis. Consequently, the major product of bovine aorta endothelial cells was converted to AB1B2. Two types of intracellular precursors were identified for each laminin-related polypeptide. Since the precursors in a given complex were synchronized with regard to maturation, the assembly of AB1B2 and A'B1B2 complexes was suggested to occur at an early step of intracellular processing.
CT Check Tags: Animal; In Vitro; Support, Non-U.S. Gov't
Cattle
Cells, Cultured
*Endothelium, Vascular: ME, metabolism
Fibroblast Growth Factors: PD, pharmacology
Glycosylation: DE, drug effects
*Laminin: ME, metabolism
Laminin: UL, ultrastructure
Macromolecular Systems
*Medroxyprogesterone: PD, pharmacology
Molecular Weight
Neovascularization, Pathologic
*Progesterone: PD, pharmacology
Protein Precursors: ME, metabolism
Transforming Growth Factor beta: PD, pharmacology
Tunicamycin: PD, pharmacology
RN **11089-65-9 (Tunicamycin)**; 520-85-4 (Medroxyprogesterone); 57-83-0 (Progesterone); 62031-54-3 (Fibroblast Growth Factors)
CN 0 (Laminin); 0 (Macromolecular Systems); 0 (Protein Precursors); 0 (Transforming Growth Factor beta)

L164 ANSWER 10 OF 13 MEDLINE
AN 87000712 MEDLINE
DN 87000712 PubMed ID: 3019419
TI Catabolic properties of aglycofibrinogen synthesized by **tunicamycin**-treated human hepatoma (HepG2) cells and rabbit hepatocytes.
AU Barsigian C; Gilman P; Base W; Fish S; Schaeffer A; **Martinez J**
NC HL-07371 (NHLBI)
HL-20092 (NHLBI)
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1986 Oct 1) 883 (3) 552-8.
Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 198611
ED Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19861107
AB Human hepatoma cell (HepG2) or rabbit hepatocyte monolayers were incubated with [35S]methionine in presence or absence of **tunicamycin**, a potent inhibitor of asparagine-linked glycosylation. The 35S-labeled nonglycosylated and control fibrinogens purified from the media were used to evaluate the influence of the oligosaccharide on the catabolic properties of this glycoprotein. Plasmin, pronase, cathepsin D or cathepsin B each degraded the nonglycosylated and control fibrinogens similarly, as evidenced by the release of trichloroacetic acid-soluble radioactivity and by SDS-polyacrylamide gel electrophoresis and autoradiography of plasmic digests. Nonglycosylated and control fibrin clots also showed no differences in susceptibility to plasmic digestion. The two forms of fibrinogen demonstrated the same plasma half-life in rabbits. These data indicate that the oligosaccharide does not influence the proteolytic stability or the in vivo plasma survival of fibrinogen, and suggest that other biochemical determinants may influence the catabolic properties of this molecule.
CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Blood Coagulation
Carcinoma, Hepatocellular: ME, metabolism
*Fibrinogen: ME, metabolism
Hydrolysis
*Liver: ME, metabolism
Liver Neoplasms
Methionine: ME, metabolism
Oligosaccharides: PH, physiology
Rabbits
***Tunicamycin: PD, pharmacology**
RN **11089-65-9 (Tunicamycin)**; 63-68-3 (Methionine); 9001-32-5 (Fibrinogen)
CN 0 (Oligosaccharides)

L164 ANSWER 11 OF 13 MEDLINE
AN 85121852 MEDLINE
DN 85121852 PubMed ID: 2982364
TI beta-Adrenergic activation of glycosyltransferases in the dolichylmonophosphate-linked pathway of protein N-glycosylation.
AU **Banerjee D K**; Kousvelari E E; Baum B J
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1985 Jan 16) 126 (1) 123-9.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198503
ED Entered STN: 19900320
Last Updated on STN: 19980206
Entered Medline: 19850320
AB beta-Adrenoreceptor stimulation of rat parotid acinar cells increases the activity of several microsomal membrane associated, dolichylmonophosphate (Dol-P) linked glycosyltransferases. The activities of Man-P-Dol synthase and Glc-P-Dol synthase are increased by approximately 50%, and the activity of N-acetylglucosaminyl 1-phosphate transferase plus N-acetylglucosaminyl transferase increased by approximately 60%, after agonist treatment. Increases in enzyme activity are (i) independent of endogenous Dol-P levels and (ii) observed under conditions in which the specific activities of donor sugar nucleotides are kept constant.

Activation of these enzymes is specific since comparable levels of NADPH-cytochrome c reductase are found in control and agonist-treated membranes. The data thus provide the initial demonstration of neurotransmitter modulation of enzymes in the dolichol-linked pathway of protein N-glycosylation.

CT Check Tags: Animal; Male
*Dolichol Phosphates: ME, metabolism
*Hexosyltransferases: ME, metabolism
Isoproterenol: PD, pharmacology
Microsomes: EN, enzymology
Parotid Gland: EN, enzymology
*Polyisoprenyl Phosphates: ME, metabolism
Rats
Rats, Inbred Strains
*Receptors, Adrenergic, beta: ME, metabolism
Tunicamycin: PD, pharmacology

RN **11089-65-9 (Tunicamycin)**; 12698-55-4 (dolichol monophosphate); 7683-59-2 (Isoproterenol)

CN 0 (Dolichol Phosphates); 0 (Polyisoprenyl Phosphates); 0 (Receptors, Adrenergic, beta); EC 2.4.1.- (Hexosyltransferases)

L164 ANSWER 12 OF 13 MEDLINE

AN 84135836 MEDLINE

DN 84135836 PubMed ID: 6699016

TI The role of the carbohydrate moiety in the biologic properties of fibrinogen.

AU Gilman P B; Keane P; **Martinez J**

NC HL-07371 (NHLBI)
HL-20092 (NHLBI)

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1984 Mar 10) 259 (5) 3248-53.
Journal code: 2985121R. ISSN: 0021-9258.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198404

ED Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840424

AB The carbohydrate moiety of some glycoproteins influences their secretion and functional properties. We have examined the importance of the oligosaccharide chains of fibrinogen in this regard. Fibrinogen was labeled de novo by the addition to rabbit hepatocyte monolayer cultures of either 3H-amino-acids or [2-3H] mannose, in the presence or absence of **tunicamycin**, a potent inhibitor of glycosylation. Inhibition of glycosylation, which ranged from 75 to 80%, was determined by incorporation of [2-3H]mannose as quantitated by gel filtration. Synthesis and secretion of fibrinogen were quantitated by 3H-amino-acid incorporation, using anti-fibrinogen immunoaffinity column chromatography of medium and cell homogenates. **Tunicamycin** did not appreciably inhibit fibrinogen synthesis, as compared to a 30-40% inhibition of overall protein synthesis, determined by incorporation of 3H-amino-acids into trichloroacetic acid-precipitable material. There was no evidence that secretion of fibrinogen was impaired. Fibrinogen from medium was copurified by adding cold plasma fibrinogen as carrier. Nonglycosylated fibrinogen was found to be functional as demonstrated by incorporation of radioactivity into clots of the copurified material at a rate identical to that of glycosylated fibrinogen. When clotted in the presence of Ca2+ and Factor XIII, cross-linking of glycosylated and nonglycosylated fibrin was demonstrable on fluorography of sodium dodecyl sulfate-polyacrylamide gels, showing disappearance of gamma-chain and appearance of gamma-gamma-dimers.

CT Check Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.

Fibrinogen: GE, genetics
*Fibrinogen: ME, metabolism
Glycoproteins: GE, genetics
*Glycoproteins: ME, metabolism
Kinetics
Liver: DE, drug effects
Liver: ME, metabolism
Mannose: ME, metabolism
Rabbits
Tritium: DU, diagnostic use
Tunicamycin: PD, pharmacology
RN 10028-17-8 (Tritium); **11089-65-9 (Tunicamycin)**; 31103-86-3 (Mannose); 9001-32-5 (Fibrinogen)
CN 0 (Glycoproteins)

L164 ANSWER 13 OF 13 MEDLINE
AN 81052330 MEDLINE
DN 81052330 PubMed ID: 6159539
TI Interferon treatment inhibits glycosylation of a viral protein.
AU Maheshwari R K; **Banerjee D K**; Waechter C J; Olden K; Friedman R M
SO NATURE, (1980 Oct 2) 287 (5781) 454-6.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198101
ED Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19810116
AB Earlier, we reported a 30-200-fold reduction in the yield of infectious vesicular stomatitis virus (VSV) released from L cells treated with 10-30 reference units ml-1 of interferon (IFN); however, in these cultures virus particle production, as measured by VSV particle-associated viral RNA, virus nucleocapsid protein and viral transcriptase, was inhibited less than 10-fold. There was biochemical and morphological evidence of a significant reduction in glycoprotein (G) and membrane protein (M) of VSV particles released from IFN-treated cells. We compare here the effects of **tunicamycin** (TM) and IFN in L cells. Treatment with TM or IFN reduced the production of infectious VSV particles, decreased the amount of G and M proteins in VSV released from treated cells, and inhibited an early step in the formation of asparagine-linked oligosaccharide chains, the incorporation by membrane preparations from treated cells of N-acetylglucosamine into glycolipids with the properties of dolichol derivatives.
CT Dolichol Phosphates: ME, metabolism
*Glucosamine: AA, analogs & derivatives
*Glycoproteins: BI, biosynthesis
*Interferons: PD, pharmacology
***Tunicamycin: PD, pharmacology**
Uridine Diphosphate N-Acetylglucosamine: ME, metabolism
*Vesicular stomatitis-Indiana virus: DE, drug effects
*Viral Proteins: BI, biosynthesis
Virus Replication: DE, drug effects
RN **11089-65-9 (Tunicamycin)**; 3416-24-8 (Glucosamine); 528-04-1 (Uridine Diphosphate N-Acetylglucosamine); 9008-11-1 (Interferons)
CN 0 (Dolichol Phosphates); 0 (Glycoproteins); 0 (Viral Proteins)

=> d all tot

L170 ANSWER 1 OF 9 MEDLINE

AN 2001291785 MEDLINE
DN 21267675 PubMed ID: 11374442
TI Removal of N-glycans from cell surface proteins induces apoptosis by reducing intracellular glutathione levels in the rhabdomyosarcoma cell line S4MH.
AU Calle Y; Palomares T; Castro B; del Olmo M; Alonso-Varona A
CS Department of Cell Biology and Morphological Sciences, School of Medicine and Odontology, University of the Basque Country, Leioa, Vizcaya, Spain.
SO BIOLOGY OF THE CELL, **(2000)** 92 (8-9) 639-46.
Journal code: 8108529. ISSN: 0248-4900.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004
AB Expression of determined Asn-bound glycans (N-glycans) in cell surface glycoproteins regulates different processes in tumour cell biology. Specific patterns of N-glycosylation are displayed by highly metastatic cells and it has been shown that inhibition of N-glycan processing restrains cell proliferation and induces cell death via apoptosis. However, the mechanisms by which different N-glycosylation states may regulate cell viability and growth are not understood. Since malignant cells express high levels of intracellular glutathione (GSH) and a reduction of intracellular GSH induces cell death via apoptosis, we investigated whether GSH was involved in the induction of apoptosis by removal of cell surface N-glycans. We found that removal of N-glycans from cell surface proteins by treating the rhabdomyosarcoma cell line S4MH with **tunicamycin** or N-glycosidase resulted in a reduction in intracellular GSH content and cell death via apoptosis. Moreover, GSH depletion caused by the specific inhibitor of GSH synthesis BSO induced apoptosis in S4MH cells. This data indicates that adequate N-glycosylation of cell surface glycoproteins is required for maintenance of intracellular GSH levels that are necessary for cell survival and proliferation.
CT Check Tags: Human; Support, Non-U.S. Gov't
Amidohydrolases: PD, pharmacology
Antibiotics: PD, pharmacology
Apoptosis: DE, drug effects
*Apoptosis: PH, physiology
Buthionine Sulfoximine: PD, pharmacology
Cell Division: DE, drug effects
Cell Division: PH, physiology
Cell Survival: DE, drug effects
Cell Survival: PH, physiology
DNA Damage: DE, drug effects
DNA Damage: PH, physiology
Enzyme Inhibitors: PD, pharmacology
*Glutathione: DF, deficiency
Intracellular Fluid: DE, drug effects
*Intracellular Fluid: ME, metabolism
*Membrane Glycoproteins: DE, drug effects
Membrane Glycoproteins: ME, metabolism
Neoplasm Metastasis: DT, drug therapy
Neoplasm Metastasis: PP, physiopathology
Neoplasm Metastasis: PC, prevention & control
*Polysaccharides: ME, metabolism
***Rhabdomyosarcoma: DT, drug therapy**
Rhabdomyosarcoma: ME, metabolism
Rhabdomyosarcoma: PP, physiopathology
*Tumor Cells, Cultured: DE, drug effects
Tumor Cells, Cultured: ME, metabolism

Tumor Cells, Cultured: PA, pathology
Tunicamycin: PD, pharmacology
RN **11089-65-9 (Tunicamycin)**; 5072-26-4 (Buthionine Sulfoximine); 70-18-8 (Glutathione)
CN 0 (Antibiotics); 0 (Enzyme Inhibitors); 0 (Membrane Glycoproteins); 0 (Polysaccharides); EC 3.5. (Amidohydrolases); EC 3.5.1.52 (peptide-N4-(N-acetyl-beta-glucosaminyl)asparagine amidase)

L170 ANSWER 2 OF 9 MEDLINE
AN 2000343950 MEDLINE
DN 20343950 PubMed ID: 10888037
TI Inhibition of N-linked glycosylation down-regulates insulin-like growth factor-1 receptor at the cell surface and kills Ewing's sarcoma cells: therapeutic implications.
AU Girnita L; Wang M; Xie Y; Nilsson G; Dricu A; Wejde J; Larsson O
CS Department of Oncology and Pathology, Cellular and Molecular Tumor Pathology, Karolinska Hospital, Stockholm, Sweden.
SO ANTI-CANCER DRUG DESIGN, **(2000 Feb)** 15 (1) 67-72.
Journal code: 8603523. ISSN: 0266-9536.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200007
ED Entered STN: 20000810
Last Updated on STN: 20000810
Entered Medline: 20000725
AB The insulin-like growth factor-1 receptor (IGF-1R) has been shown to be of critical importance for tumor development and tumor cell survival of various types of malignancies. We have previously demonstrated that an adequate N-linked glycosylation of IGF-1R is required for its translocation to the cell surface in melanoma cells. This raises the possibility of using glycosylation inhibitors as therapeutic agents against IGF-1R-dependent malignancies. In this study we show that inhibition of N-linked glycosylation using **tunicamycin** or the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor lovastatin resulted in down-regulation of IGF-1R at the cell surface in Ewing's sarcoma cell lines (RD-ES and ES-1 cells). The down-regulation of plasma membrane-bound IGF-1R was correlated with a drastic decrease in IGF-1R autophosphorylation, suggesting biochemical inactivation of the receptor. Whereas RD-ES and ES-1 cells responded differently with regard to DNA synthesis, the decrease in IGF-1R expression was accompanied by a rapid and substantial decrease in survival of both cell lines. Our data suggest that relatively untoxic HMG-CoA reductase inhibitors (e.g. lovastatin) could have therapeutic significance in IGF-1R-dependent neoplasms like Ewing's sarcoma.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Antineoplastic Agents: PD, pharmacology
Antineoplastic Agents: TU, therapeutic use
Cell Division: DE, drug effects
Cell Survival: DE, drug effects
*Down-Regulation
Glycosylation
Lovastatin: PD, pharmacology
*Receptor, IGF Type 1: AI, antagonists & inhibitors
Receptor, IGF Type 1: ME, metabolism
Sarcoma, Ewing's: DT, drug therapy
Sarcoma, Ewing's: ME, metabolism
***Sarcoma, Ewing's: PA, pathology**
Tumor Cells, Cultured
Tunicamycin: PD, pharmacology
RN **11089-65-9 (Tunicamycin)**; 75330-75-5 (Lovastatin)
CN 0 (Antineoplastic Agents); EC 2.7.11.- (Receptor, IGF Type 1)

L170 ANSWER 3 OF 9 MEDLINE
AN 1999131910 MEDLINE
DN 99131910 PubMed ID: 9935211
TI Inhibition of N-linked glycosylation by **tunicamycin** enhances sensitivity to cisplatin in human head-and-neck carcinoma cells.
AU Noda I; Fujieda S; Seki M; Tanaka N; Sunaga H; Ohtsubo T; Tsuzuki H; Fan G K; Saito H
CS Department of Otorhinolaryngology, Fukui Medical University, Japan.
SO INTERNATIONAL JOURNAL OF CANCER, **(1999 Jan 18)** 80 (2) 279-84.
Journal code: 0042124. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990216
AB **Tunicamycin** (TM), a naturally occurring antibiotic, blocks the first step in the biosynthesis of N-linked oligosaccharides in cells. In this study, we investigated whether changes in N-linked glycosylation affect the sensitivity of head-and-neck carcinoma cell lines to cis-diaminedichloroplatinum(II) (cisplatin) in vitro and in vivo. In vitro treatment of the IMC-3 and KB cell lines with TM significantly decreased the 50% inhibitory concentration (IC50) of cisplatin, as determined by the MTT assay (24.15 to 10.97 microg/ml, $p < 0.05$). In addition, TM significantly decreased the IC50 of cisplatin against established cisplatin-resistant IMC-3/CR cells (>100 to 14.4 microg/ml, $p < 0.05$) to levels similar to those against parental IMC-3 cells. TM treatment decreased the number of Con A- and L-PHA-binding sites on the surface of tumor cells but had no effect on the intracellular platinum concentration. Induction of apoptosis in vitro by TM plus cisplatin in combination was increased compared with that by cisplatin alone. Furthermore, in vivo administration of TM plus cisplatin in combination significantly inhibited local tumor growth in the cisplatin-resistant in vivo C3H/He mouse model as compared with the control group ($p < 0.05$) and increased in vivo apoptosis of tumor cells. Our results suggest that the manipulation of glycosylation by TM in tumor cells might be a useful therapeutic strategy for successful chemotherapy using cisplatin against head-and-neck cancer.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Antibiotics: TU, therapeutic use
*Antineoplastic Agents: TU, therapeutic use
Apoptosis: DE, drug effects
Carbohydrate Conformation
*Cisplatin: TU, therapeutic use
Drug Synergism
Glycosylation
***Head and Neck Neoplasms: DT, drug therapy**
Head and Neck Neoplasms: PA, pathology
Mice
Mice, Inbred C3H
Tumor Cells, Cultured
***Tunicamycin: TU, therapeutic use**
RN **11089-65-9 (Tunicamycin)**; 15663-27-1 (Cisplatin)
CN 0 (Antibiotics); 0 (Antineoplastic Agents)

L170 ANSWER 4 OF 9 MEDLINE
AN 1998168373 MEDLINE
DN 98168373 PubMed ID: 9507530
TI **Tunicamycin** in combination with retinoic acid synergistically inhibits cell growth while decreasing palmitoylation and enhancing retinoylation of proteins in the human breast cancer cell line MCF-7.

AU Takahashi N; Iwahori A; Breitman T R; Fukui T
CS Department of Health Chemistry, Hoshi University, Tokyo, Japan..
t-noriko@hoshi.ac.jp
SO ONCOLOGY RESEARCH, **(1997)** 9 (10) 527-33.
Journal code: 9208097. ISSN: 0965-0407.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980604
AB All-trans-Retinoic acid (RA) induces differentiation and inhibits growth of many tumor types. Whereas the RA nuclear receptors mediate genomic effects of RA, there also are many nongenomic effects that do not have defined mechanisms. Some nongenomic effects of RA may involve retinoylation (RA acylation), a posttranslational modification of proteins occurring in many eukaryotic cell lines including the human breast cancer cell line MCF-7. To gain further knowledge of the role(s) of retinoylation, we studied the effects of **tunicamycin** (TM), an inhibitor of both protein N-glycosylation and palmitoylation, on growth and retinoylation in MCF-7 cells. We found that RA or TM alone inhibited growth of MCF-7 cells. Combinations of RA and TM inhibited growth synergistically. TM increased retinoylation and decreased palmitoylation. These results suggest that increased retinoylation and decreased glycosylation and palmitoylation may play a role in the synergistic inhibition of cell growth by combinations of TM and RA in MCF-7 cells. Furthermore, our results suggest that combinations of TM and RA may have clinical utility.
CT Check Tags: Human; Support, Non-U.S. Gov't
Acylation
*Antineoplastic Combined Chemotherapy Protocols: TU, therapeutic use
***Breast Neoplasms: DT, drug therapy**
Breast Neoplasms: PA, pathology
Cell Division: DE, drug effects
Drug Synergism
*Neoplasm Proteins: ME, metabolism
Palmitic Acid: ME, metabolism
Tretinoin: AD, administration & dosage
Tretinoin: ME, metabolism
Tumor Cells, Cultured
Tunicamycin: AD, administration & dosage
RN **11089-65-9 (Tunicamycin)**; 302-79-4 (Tretinoin); 57-10-3 (Palmitic Acid)
CN 0 (Antineoplastic Combined Chemotherapy Protocols); 0 (Neoplasm Proteins)

L170 ANSWER 5 OF 9 MEDLINE
AN 94115088 MEDLINE
DN 94115088 PubMed ID: 8286860
TI Cell cycle-specific growth inhibition of human breast cancer cells induced by metabolic inhibitors.
AU Larsson O
CS Department of Tumor Pathology, Karolinska Institutet, Karolinska Hospital, Stockholm, Sweden.
SO GLYCOBIOLOGY, **(1993 Oct)** 3 (5) 475-9.
Journal code: 9104124. ISSN: 0959-6658.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199402
ED Entered STN: 19940312

Last Updated on STN: 19970203
Entered Medline: 19940224

AB Proliferation of exponentially growing breast cancer cells (line Hs578T) was blocked specifically in G1 by 3-hydroxy-3-methylglutaryl Coenzyme A (HMG CoA) reductase inhibition, as well as by inhibition of N-linked glycosylation. As a consequence of these inhibitory conditions, the cells were synchronized in the G1 stage of the cell cycle. The similarities in the kinetic responses point to the possibility that the two different types of metabolic inhibitions block cell cycle progression by common mechanisms. One possibility is that the inhibition of HMG CoA reductase activity also leads to a depressed rate of N-linked glycosylation, which in turn may constitute the critical event for cell cycle progression and cell growth. In order to investigate whether this relationship exists in breast cancer cells, cells synchronized in G1 by mevinolin (an inhibitor of HMG CoA reductase) were used. Upon addition of mevalonate, whose endogenous synthesis is catalysed by HMG CoA reductase, the cells entered S phase after a 4 h pre-replicative period. Mevalonate stimulation also led to a rapid and substantial increase in N-linked glycosylation, measured by determining the uptake of radioactive glucosamine. This metabolic event was found to be of critical importance for the initiation of DNA synthesis. However, as soon as the cells had entered S phase, they were independent of the level of N-linked glycosylation.

CT Check Tags: Female; Human; Support, Non-U.S. Gov't
*Antimetabolites: PD, pharmacology
***Breast Neoplasms: DT, drug therapy**
Breast Neoplasms: ME, metabolism
Breast Neoplasms: PA, pathology
Cell Cycle: DE, drug effects
Cell Division: DE, drug effects
DNA, Neoplasm: BI, biosynthesis
Glycosylation: DE, drug effects
Hydroxycholesterols: PD, pharmacology
Hydroxymethylglutaryl-CoA Reductase Inhibitors
Kinetics
Lovastatin: PD, pharmacology
Mevalonic Acid: ME, metabolism
Mevalonic Acid: PD, pharmacology
Neoplasm Proteins: ME, metabolism
Tumor Cells, Cultured: DE, drug effects
Tumor Cells, Cultured: ME, metabolism
Tumor Cells, Cultured: PA, pathology
Tunicamycin: PD, pharmacology

RN **11089-65-9 (Tunicamycin)**; 150-97-0 (Mevalonic Acid); 2140-46-7 (25-hydroxycholesterol); 75330-75-5 (Lovastatin)

CN 0 (Antimetabolites); 0 (DNA, Neoplasm); 0 (Hydroxycholesterols); 0 (Hydroxymethylglutaryl-CoA Reductase Inhibitors); 0 (Neoplasm Proteins)

L170 ANSWER 6 OF 9 MEDLINE
AN 87148868 MEDLINE
DN 87148868 PubMed ID: 3469745
TI The effect of **tunicamycin** on target cell susceptibility to natural killer cell cytotoxicity.
AU Nose M; Gidlund M; Hosein Z; Axberg I; Wigzell H; Yogeeswaran G
SO SCANDINAVIAN JOURNAL OF IMMUNOLOGY, **(1987 Feb)** 25 (2) 149-57. Journal code: 0323767. ISSN: 0300-9475.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198703
ED Entered STN: 19900303
Last Updated on STN: 19970203
Entered Medline: 19870330

AB Several sets of data indicate the possibility that carbohydrate moieties on the target cell are important structures in natural killer (NK) cell-mediated lysis. Striking changes in the NK susceptibility of targets can be induced in several systems involving in vitro differentiation of tumour cell lines. The effect on target cells of the glycosylation inhibitor **tunicamycin**, which acts by blocking the dolichol-dependent asparagine-linked glycosylation pathway was investigated. Using several different tumour cell lines we can conclude that: asparagine-linked carbohydrate chains do not contribute directly to NK susceptibility, induced differentiation may or may not be linked with a change in NK susceptibility, and secondary changes caused by **tunicamycin** treatment may lead to alterations in the gangliosides, a finding that is positively correlated with decreased NK susceptibility.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Binding, Competitive
Cell Line
Cell Membrane: ME, metabolism
Cytotoxicity, Immunologic
Gangliosides: ME, metabolism
Killer Cells, Natural: IM, immunology
Killer Cells, Natural: RE, radiation effects
Kinetics
Leukemia, Myeloid: DT, drug therapy
Leukemia, Myeloid: IM, immunology
***Leukemia, Myeloid: PA, pathology**
Mice
Time Factors
***Tunicamycin: PD, pharmacology**

RN **11089-65-9 (Tunicamycin)**
CN 0 (Gangliosides)

L170 ANSWER 7 OF 9 MEDLINE
AN 83155250 MEDLINE
DN 83155250 PubMed ID: 6339042
TI Biochemical effects and therapeutic potential of **tunicamycin** in murine L1210 leukemia.
AU Morin M J; Bernacki R J
NC CA 13038 (NCI)
SO CANCER RESEARCH, **(1983 Apr)** 43 (4) 1669-74.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198305
ED Entered STN: 19900318
Last Updated on STN: 19970203
Entered Medline: 19830505

AB **Tunicamycin**, an antibiotic which specifically inhibits the dolichol-mediated synthesis of glycoproteins, significantly decreased the incorporation of tritiated D-mannose and D-glucosamine into L1210 ascites leukemia cell glycoproteins at concentrations which affected the biosynthesis of proteins minimally. Mice receiving inoculations of L1210 cells pretreated with 10 microM **tunicamycin** in vitro survived nearly twice as long as did mice receiving implants of untreated tumor cells. A nonlethal dose of X-irradiation (350 rads) to mice 24 hr prior to receiving their inoculation of **tunicamycin**-treated L1210 cells prevented this increase in life span. Thirty-eight % of the long-term surviving mice which received 1 X 10(5) L1210 cells pretreated with 10 microM **tunicamycin** in vitro were then resistant to a subsequent challenge with 10(6) untreated L1210 ascites cells. Direct i.p. administration of **tunicamycin** to mice resulted in potent liver toxicity (50% lethal dose, 2.0 mg/kg) which obviated any therapeutic

efficacy when administered to L1210 ascites tumor-bearing mice. The administration of nontoxic levels of D-mannose prior to the administration of **tunicamycin** decreased the toxicity of the antibiotic in vivo and, when combined with D-mannose in vitro, exhibited cytotoxic additivity in terms of the inhibition of L1210 leukemic cell growth. A therapeutic regimen incorporating a 24-hr infusion of the sugar prior to multiple administrations of **tunicamycin** gave evidence of a small therapeutic response in terms of the survival of tumor-bearing mice. These results suggest that **tunicamycin**, an inhibitor of glycoprotein biosynthesis, might be able to alter tumor cell growth and immunogenicity provided that host liver toxicity is diminished.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Glucosamine: AA, analogs & derivatives
Glycoproteins: BI, biosynthesis
Immune Tolerance: RE, radiation effects
Kinetics
***Leukemia L1210: DT, drug therapy**
Leukemia L1210: ME, metabolism
Mannose: PD, pharmacology
Mice
Mice, Inbred DBA
Neoplasm Proteins: BI, biosynthesis
Protein Precursors: BI, biosynthesis
***Tunicamycin: TU, therapeutic use**
Tunicamycin: TO, toxicity
Whole-Body Irradiation

RN **11089-65-9 (Tunicamycin)**; 31103-86-3 (Mannose); 3416-24-8 (Glucosamine)

CN 0 (Glycoproteins); 0 (Neoplasm Proteins); 0 (Protein Precursors)

L170 ANSWER 8 OF 9 MEDLINE

AN 83132785 MEDLINE

DN 83132785 PubMed ID: 6186542

TI **Tunicamycin** reversibly inhibits the terminal differentiation of teratocarcinoma stem cells to endoderm.

AU Grabel L B; Martin G R

SO DEVELOPMENTAL BIOLOGY, **(1983 Jan)** 95 (1) 115-25.
Journal code: 0372762. ISSN: 0012-1606.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198304

ED Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830415

AB The differentiation of aggregates of certain teratocarcinoma stem cell lines begins with the formation of an outer layer of primary endoderm cells characterized by the production of plasminogen activator and the absence of histochemically detectable alkaline phosphatase activity. After several days of culture these outer cells develop into a mixture of two types of terminally differentiated endoderm: parietal endoderm which produces a thick layer of underlying basement membrane and visceral endoderm which produces alpha-fetoprotein (AFP). We report here that in the presence of **tunicamycin**, a drug that inhibits glycosylation of N-asparagine linked glycoproteins, a primary endoderm-like cell is formed which is alkaline phosphatase negative and plasminogen activator positive. However, terminal differentiation of these cells is inhibited as manifested by the lack of accumulation of a thick basement membrane and the absence of immunologically detected AFP. Such inhibition is reversible following removal of the **tunicamycin**. Terminal differentiation of endoderm depends, therefore, upon N-asparagine linked glycoproteins.

CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't

Alkaline Phosphatase: ME, metabolism
*Cell Differentiation: DE, drug effects
Cells, Cultured
Endoderm: DE, drug effects
*Glucosamine: AA, analogs & derivatives
Glycosides: ME, metabolism
Mice
Neoplasms, Experimental: DT, drug therapy
Plasminogen Activators: ME, metabolism
***Teratoma: DT, drug therapy**
Teratoma: ME, metabolism
Teratoma: PA, pathology
***Tunicamycin: PD, pharmacology**
alpha-Fetoproteins: ME, metabolism
RN **11089-65-9 (Tunicamycin)**; 3416-24-8 (Glucosamine)
CN 0 (Glycosides); 0 (alpha-Fetoproteins); EC 3.1.3.1 (Alkaline Phosphatase); EC 3.4.21.- (Plasminogen Activators)

L170 ANSWER 9 OF 9 MEDLINE
AN 82160211 MEDLINE
DN 82160211 PubMed ID: 6950722
TI Effects of **tunicamycin** on anthracycline resistance in P388 murine leukemia cells.
AU Chou T H; Kessel D
NC 05384-10 (NCI)
CA 23243
SO BIOCHEMICAL PHARMACOLOGY, **(1981 Nov 15)** 30 (22) 3134-6.
Journal code: 0101032. ISSN: 0006-2952.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198205
ED Entered STN: 19900317
Last Updated on STN: 19970203
Entered Medline: 19820512
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
Antibiotics, Anthracycline
*Antibiotics, Antineoplastic: PD, pharmacology
Cell Line
Daunorubicin: ME, metabolism
Daunorubicin: PD, pharmacology
Doxorubicin: PD, pharmacology
Drug Resistance
*Glucosamine: AA, analogs & derivatives
Glycoproteins: BI, biosynthesis
***Leukemia P388: DT, drug therapy**
Leukemia P388: ME, metabolism
***Leukemia, Experimental: DT, drug therapy**
Mice
Naphthacenes: PD, pharmacology
***Tunicamycin: PD, pharmacology**
Tunicamycin: TU, therapeutic use
RN **11089-65-9 (Tunicamycin)**; 20830-81-3 (Daunorubicin); 23214-92-8 (Doxorubicin); 3416-24-8 (Glucosamine)
CN 0 (Antibiotics, Anthracycline); 0 (Antibiotics, Antineoplastic); 0 (Glycoproteins); 0 (Naphthacenes)

=> d his

(FILE 'HOME' ENTERED AT 13:36:32 ON 08 APR 2003)
SET COST OFF

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     FILE 'REGISTRY' ENTERED AT 13:36:44 ON 08 APR 2003
                ACT OWENS779/A
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L1             9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (TUNICAMYCIN/CN OR "TUNICAMYC
                ---------
L2             9 SEA FILE=REGISTRY ABB=ON  PLU=ON  (TUNICAMYCIN/CN OR "TUNICAMYC
L3               STR
L4             1 S L3
L5            72 S L3 FUL
                 SAV L5 OWENS779B/A
L6               STR L3
L7            63 S L6 CSS FUL SUB=L5
                 SAV L7 OWENS779C/A
L8             9 S L5 NOT L1,L2,L7

     FILE 'HCAPLUS' ENTERED AT 13:44:37 ON 08 APR 2003
L9           684 S L1
L10            9 S L2
L11           39 S L7
L12            8 S L8
                 E TUNICAMYCIN
L13         3256 S E3-E7
                 E TUNICAM
L14           42 S E4-E9
L15           45 S L13,L14(S)(A1 OR A2 OR B1 OR B2 OR C1 OR C2 OR D1 OR D2)
L16         3285 S L9-L15
                 E ANGIOGEN/CT
L17        10311 S E4-E9
                 E E4+ALL
L18         8360 S E5+NT
                 E E10+ALL
L19         3109 S E4+NT
                 E E7+ALL
L20         1687 S E3,E4,E2+NT
                 E RETINOPATH/CT
                 E E4+ALL
L21         2695 S E2
                 E DIABET/CT
                 E E55+ALL
L22         1568 S E2
                 E ATHEROSLCEROTIC PLAQUE/CT
                 E ATHEROSCLEROTIC PLAQUE/CT
                 E ATHEROSCLERO/CT
                 E E4+ALL
L23        24850 S E7-E9,E6+NT
                 E E5+ALL
L24        28214 S E5+NT
                 E E11+ALL
L25         5727 S E4
                 E SCLERODERM/CT
                 E E5+ALL
L26         1615 S E2
                 E HYPERTROPH/CT
                 E E9+ALL
L27          148 S E2
                 E VASCULAR ADHESION/CT
                 E ADHESION/CT
                 E E19+ALL
L28         7313 S VASCULAR?(L)ADHESION
                 E ANGIOFIBROMA/CT
                 E E3+ALL
L29           76 S E2
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                E TRACHOMA/CT
                E NEOVASCULAR/CT
                E E4+ALL
L30          1809 S E2
L31           187 S E8,E9
                E GLAUCOMA/CT
L32          3130 S E3-E12
                E E4+ALL
L33          3044 S E5,E4+NT
                E E10+ALL
L34          1018 S E3
                E THROMBOSIS/CT
L35          8485 S E3-E21
                E E3+ALL
L36          8562 S E4+NT
                E E12+ALL
L37         17689 S E5,E4+NT
                E E12+ALL
L38         17325 S E7+NT
L39         29065 S E16+NT
L40           839 S E17+NT
L41          1449 S E20+NT OR E24+NT
                E E22+ALL
L42          8562 S E4+NT
                E E17+ALL
L43          2009 S E4
                E RESTENOSIS/CT
                E E3+ALL
L44          2839 S E2,E3
                E OSTEOPOROSIS/CT
L45          8203 S E3-E9
                E E+ALL
                E OSTEOPOROSIS/CT
                E E3+ALL
L46          8204 S E6+NT
                E BONE DENSITY/CT
                E E2+ALL
L47           969 S E2
                E BONE/CT
L48         48248 S E3
L49          5183 S E56,E57
L50          6347 S E186
L51          2261 S E225
L52          6191 S E226
L53          5662 S E249
L54           999 S E250,E251,E252
L55          1007 S E253
                E MACULAR DEGENERATION/CT
                E E3+ALL
L56           738 S E2
                E ARTHRITIS/CT
L57         12290 S E3-E25
                E E3+ALL
L58         21540 S E6+NT
                E E19+ALL
L59          4641 S E5,E4+NT
                E E7+ALL
                E E20+ALL
L60          1693 S E5,E4+NT
                E E8+ALL
L61         11025 S E10,E11,E9+NT
                E HEMANGIOMAS/CT
                E HEMANGIOMA/CT
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                E E3+ALL
L62          363 S E2
                E PSORIASIS/CT
L63         6798 S E3-E5
                E E3+ALL
L64         6798 S E4
                E E4
                E E7+ALL
L65          220 S E2
                E TUMOR/CT
L66          728 S E3
                E E3+ALL
L67        86974 S E2
                E E2+ALL
L68       230289 S E3-E7,E2+NT
                E E105+ALL
L69       155846 S E4,E3+NT
L70       273606 S NEOPLAS?/CW
L71          373 S L16 AND L17-L70
                E BANERJEE D/AU
L72          564 S E3,E7,E46-E48
                E MARTINEZ J/AU
L73          602 S E3-E8
                E MARTINEZ JUAN/AU
L74           30 S E3-E5
L75            5 S L72-L74 AND L16
L76            2 S L75 AND L71
L77            5 S L75,L76
L78           15 S (L1 OR L2 OR L7 OR L8) (L) (THU OR PAC OR PKT)/RL AND L71
L79            5 S L16 AND ?ANGIOGEN?
L80            4 S L79 NOT HYPOXIA
L81            1 S L16 AND ?RETINOPATH?
L82           10 S L16 AND ?DIABET?
L83            0 S L82 AND (EYE OR RETINA OR RETINAL)
L84            0 S L82 AND L81
L85            0 S L78 AND L81,L82
L86            9 S L16 AND (?ATHEROSCLER? OR ?ARTERIOSCLER?)
L87           55 S L16 AND (?SCLERODERM? OR HYPERTROPH? OR SCAR? OR VASCULAR?(L)
L88            0 S L78 AND L87,L86
L89          655 S L16 AND (?NEOPLAS? OR ?TUMOR? OR ?MALIGN? OR ?CANCER? OR ?CAR
L90           14 S L78 AND L89
L91          755 S L78-L90,L71 AND (PD<=20000209 OR PRD<=20000209 OR AD<=2000020
                SEL RN L77

     FILE 'REGISTRY' ENTERED AT 14:22:10 ON 08 APR 2003
L92           11 S E1-E11
L93            1 S L92 AND L1,L2,L5,L7,L8
L94           10 S L92 NOT L93

     FILE 'HCAPLUS' ENTERED AT 14:27:14 ON 08 APR 2003
                E NUCLEOSIDE/CT
L95         1025 S E34
                E E14+ALL
L96          169 S E51
L97            1 S L95,L96 AND L91

     FILE 'HCAPLUS' ENTERED AT 14:28:55 ON 08 APR 2003
                S GLUCOSAMINE/CN

     FILE 'REGISTRY' ENTERED AT 14:28:55 ON 08 APR 2003
L98            1 S GLUCOSAMINE/CN

     FILE 'HCAPLUS' ENTERED AT 14:28:55 ON 08 APR 2003
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L99        5131 S L98
L100      18777 S GLUCOSAMINE
L101         90 S L91 AND L99,L100

     FILE 'REGISTRY' ENTERED AT 14:29:28 ON 08 APR 2003
L102          1 S 7512-17-6

     FILE 'HCAPLUS' ENTERED AT 14:30:02 ON 08 APR 2003
L103       5041 S L102
L104      13257 S ?ACETYLGLUCOSAMINE? OR ACETYL(1W)GLUCOSAMINE
L105         39 S L91 AND L103,L104
L106        116 S L101,L105
L107          3 S L78 AND L106
L108          7 S L77,L107
L109        113 S L91 AND (1 OR 63)/SC,SX
L110         30 S L106 AND L109
L111         13 S L110 AND (LECTIN OR HL OR VIRUS OR STRESS OR NEWCASTLE OR VIT
L112         17 S L110 NOT L111
L113         20 S L108,L112
L114         21 S L91 AND DOLICHOL
L115          3 S L91 AND FACTOR VIII C

     FILE 'REGISTRY' ENTERED AT 14:40:58 ON 08 APR 2003
L116          1 S 11029-02-0
L117          2 S 70431-08-2 OR 113189-02-9
L118          1 S 62213-44-9

     FILE 'HCAPLUS' ENTERED AT 14:43:13 ON 08 APR 2003
L119       2368 S L116 OR L117 OR L118
L120          7 S L119 AND L91
L121         38 S L113-L115,L120 AND L9-L91,L95-L97,L99-L101,L103-L115,L119,L
L122         37 S L121 AND L91
L123         38 S L121,L122
L124         25 S L123 AND (?ANGIOGEN? OR ?DOLICH? OR FACTOR VIII)
L125         13 S L123 NOT L124

     FILE 'REGISTRY' ENTERED AT 14:47:36 ON 08 APR 2003

     FILE 'HCAPLUS' ENTERED AT 14:48:11 ON 08 APR 2003

     FILE 'MEDLINE' ENTERED AT 14:48:31 ON 08 APR 2003
L126       2105 S L1 OR L2 OR L5
               E TUNICAM
L127       3231 S E4-E13
L128       3231 S L126,L127
L129       3068 S L128 AND PY<=2000
               E ANGIOGENESIS/CT
               E E28+ALL
L130       1452 S E32
L131          0 S L129 AND L130
L132          7 S L129 AND ?ANGIOGEN?
               E DIABETIC RETINOPATHY/CT
               E E3+ALL
L133          0 S L129 AND E14+NT
               E ATHEROSCLER/CT
               E E8+ALL
               E E2+ALL
L134          3 S L129 AND E5+NT
               E SCLERODERMA/CT
               E E43+ALL
L135          0 S L129 AND E7+NT
               E SCLERODERMA/CT
L136          0 S L129 AND E4+NT
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                E HYPERTROPHIC SCARRING/CT
                E E4+ALL
L137          0 S L129 AND E2+NT
                E VASCULAR ADHESION/CT
L138          5 S L129 AND VASCULAR(L)ADHESION
                E ANGIOFIBROMA/CT
L139          0 S L129 AND E3+NT
                E TRACHOMA/CT
                E E3+ALL
L140          0 S L129 AND E35+NT
                E NEOVASCULARIZATION/CT
L141          4 S L129 AND (E8+NT OR E46+NT)
                E E53+ALL
L142          0 S L129 AND E2+NT
                E NEOVASCULARIZATION/CT
                E E7+ALL
L143          0 S L129 AND E2+NT
                E GLAUCOMA/CT
L144          0 S L129 AND E3+NT
                E THROMBOSIS/CT
L145          2 S L129 AND E3+NT
                E RESTENOSIS/CT
                E E4+ALL
L146          0 S L129 AND E2+NT
L147          0 S L129 AND E4+NT
                E OSTEOPOROSIS/CT
L148          0 S L129 AND E3+NT
                E BONE DENSITY/CT
L149          0 S L129 AND E3+NT
                E BONE DEMINERALIZATION/CT
                E E4+ALL
L150          0 S L129 AND E2+NT
                E BONE REMINERAL/CT
                E BONE REGENERATION/CT
L151          0 S L129 AND E3+NT
                E MACULAR DEGENERATION/CT
L152          0 S L129 AND E3+NT
                E ARTHRITIS/CT
L153          4 S L129 AND E3+NT
                E HEMANGIOMAS/CT
                E E3+ALL
L154          1 S L129 AND E2+NT
                E PSORIASIS/CT
L155          0 S L129 AND E3+NT
                E TUMOR/CT
                E E3+ALL
L156        546 S L129 AND E2+NT
L157          3 S L132-L155 AND L156
L158          9 S L132,L157
                E BANERJEE D/AU
L159        401 S E3,E5
                E MARTINEZ J/AU
L160       1195 S E3-E8
                E MARTINEZ JUAN/AU
L161          2 S E3
                E BANERJEE DIPAK/AU
L162          3 S E4,E5
L163          7 S L159-L162 AND L128
L164         13 S L158,L163

     FILE 'MEDLINE' ENTERED AT 15:01:02 ON 08 APR 2003
L165    1424959 S C4./CT
L166        341 S L165/MAJ AND L129
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L167          12 S L165(L)DT/CT AND L166
L168           9 S L167 AND TUNICAMYCIN/CT
L169          12 S L167 NOT L164
L170           9 S L168 AND L169

=> fil biosis
FILE 'BIOSIS' ENTERED AT 15:04:17 ON 08 APR 2003
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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 2 April 2003 (20030402/ED)


=> d all tot

L177 ANSWER 1 OF 5  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN   2000:514172  BIOSIS
DN   PREV200000514172
TI   Tunicamycin inhibits angiogenesis by ER stress.
AU   Martinez, Juan A. (1); Banerjee, Dipak K. (1)
CS   (1) Department of Biochemistry, School of Medicine, University of Puerto
     Rico, San Juan, 00936-5067 Puerto Rico
SO   Glycobiology, (October, 2000) Vol. 10, No. 10, pp. 1131. print.
     Meeting Info.: 5th Annual Conference of the Society for Glycobiology
     Boston, Massachusetts, USA November 08-11, 2000 Society for Glycobiology
     . ISSN: 0959-6658.
DT   Conference
LA   English
SL   English
CC   Biochemical Studies - Nucleic Acids, Purines and Pyrimidines  *10062
     General Biology - Symposia, Transactions and Proceedings of Conferences,
     Congresses, Review Annuals  *00520
     Biochemical Studies - General  *10060
     Biochemical Studies - Proteins, Peptides and Amino Acids  *10064
     Endocrine System - General  *17002
IT   Major Concepts
        Biochemistry and Molecular Biophysics
IT   Parts, Structures, & Systems of Organisms
        endoplasmic reticulum
IT   Chemicals & Biochemicals
        cAMP [cyclic AMP]; dolichol; factor VIII:C; fibroblast growth factor-2;
        tunicamycin: angiogenesis inhibitor
IT   Miscellaneous Descriptors
          angiogenesis; apoptosis; capillary endothelial cell line;
        cell cycle; Meeting Abstract,
RN   60-92-4 (CYCLIC AMP)
     11029-02-0 (DOLICHOL)
     106096-93-9 (FIBROBLAST GROWTH FACTOR-2)
       11089-65-9 (TUNICAMYCIN)

L177 ANSWER 2 OF 5  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN   1999:300398  BIOSIS
DN   PREV199900300398
TI   cAMP blocks apoptosis during tunicamycin-induced inhibition of
     angiogenesis in vitro.
AU   Martinez, J. A. (1); Banerjee, D. K. (1)
CS   (1) Dept. Biochemistry, School of Med. Univ. of Puerto Rico, San Juan, PR,
     00935 USA
SO   FASEB Journal, (April 23, 1999) Vol. 13, No. 7, pp. A1436.
     Meeting Info.: Annual Meeting of the American Societies for Experimental
```

Biology on Biochemistry and Molecular Biology 99 San Francisco, California, USA May 16-20, 1999 American Societies for Experimental Biology
. ISSN: 0892-6638.
DT Conference
LA English
CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Cardiovascular System - Physiology and Biochemistry *14504
Enzymes - Physiological Studies *10808
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Mammalia - Unspecified 85700
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology
IT Parts, Structures, & Systems of Organisms
vascular endothelial cells: circulatory system
IT Chemicals & Biochemicals
cAMP [cyclic AMP]; Dol-P-Man synthase: activation
IT Miscellaneous Descriptors
angiogenesis: in-vitro, **tunicamycin**-induced inhibition; apoptosis: blockade; Meeting Abstract
ORGN Super Taxa
Mammalia: Vertebrata, Chordata, Animalia
ORGN Organism Name
mammal (Mammalia)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates
RN **11089-65-9** (**TUNICAMYCIN**)
60-92-4 (CYCLIC AMP)
9031-57-6 (SYNTHASE)

L177 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:173057 BIOSIS
DN PREV199900173057
TI Expression of Glc3Man9GlcNAc2-PP-Dol is a prerequisite for capillary endothelial cell proliferation.
AU **Martinez, Juan A.**; Torres-Negron, Ivette; Amigo, Lilia A.; **Banerjee, Dipak K. (1)**
CS (1) Department of Biochemistry, School of Medicine, University of Puerto Rico, San Juan, PR, 00936-5067 USA
SO Cellular and Molecular Biology (Noisy-Le-Grand), (**Feb., 1999**) Vol. 45, No. 1, pp. 137-152.
DT Article
LA English
AB Protein N-glycosylation has been proposed to be intimately involved in the migration, proliferation and differentiation of endothelial cells. Using a synchronized, non-transformed capillary endothelial cell line from bovine adrenal medulla as a model, and the N-glycosylation inhibitor, **tunicamycin**, we have elucidated the molecular basis of the dolichol pathway in the **angiogenic** process. The synchronized culture required approximately 68 hrs. to complete one cell cycle, cells spending nearly 36 hrs. in G1 phase, 8 hrs. in S phase and 24 hrs. in G2 + M phase when maintained in 2% fetal bovine serum (heat-inactivated). The cell cycle however, was shortened due to a reduction of the G1 phase by 12-16 hrs. when the serum concentration was increased to 10%, or when betaFGF (1 or 10 nanogram) was added into the culture media containing 2% serum. Light microscopy and scanning electron microscopy both supported these proliferative responses. Serum concentration below 2% arrested cell proliferation and induced capillary lumen-like structure formation with 48 hrs. Expression of the blood clotting antigen factor VIII (a Mr 270,000

dalton N-linked glycoprotein and a marker of our endothelial cells) preceded the endothelial cell proliferation and established a temporal relationship. **Tunicamycin**, an inhibitor of Glc3Man9GlcNAc2-PP-Dol biosynthesis, a prerequisite for N-linked protein glycosylation in the ER- inhibited the cell growth and proliferation in a time and dose-dependent manner with a concomitant accumulation of immunopositive, non-glycosylated factor VIII:C in the conditioned media. **Tunicamycin** also caused surface blebbing and induction of programmed cell death (PCD)(apoptosis) within 32 hrs. Absence of cellular growth and proliferation, surface blebbing and the induction of PCD in the presence of **tunicamycin**, provided conclusive evidence that normal expression of Glc3Man9GlcNAc2-PP-Dol is an essential event for capillary proliferation during **angiogenesis**.

CC Cardiovascular System - Physiology and Biochemistry *14504
Microscopy Techniques - Cytology and Cytochemistry *01054
Microscopy Techniques - Electron Microscopy *01058
Cytology and Cytochemistry - Animal *02506
Developmental Biology - Embryology - Morphogenesis, General *25508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506

BC Bovidae 85715

IT Major Concepts
Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Methods and Techniques

IT Parts, Structures, & Systems of Organisms
capillary endothelial cell: circulatory system

IT Chemicals & Biochemicals
factor VIII:C

IT Methods & Equipment
cell culture: cell culture method, cell culture techniques; flow cytometry: analytical method, cytophotometry: CT, cytophotometry: CB; light microscopy: microscopy method, microscopy: CB, microscopy: CT; scanning electron microscopy: electron microscopy: CB, electron microscopy: CT, microscopy method; Autoscan ETEC scanning electron microscope: equipment; Nikon Alphashot inverted microscope: equipment

IT Miscellaneous Descriptors
angiogenesis; apoptosis; cell cycle

ORGN Super Taxa
Bovidae: Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
bovine (Bovidae)

ORGN Organism Superterms
Animals; Artiodactyls; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates

RN 113189-02-9 (FACTOR VIII:C)

L177 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1995:462794 BIOSIS
DN PREV199598477094
TI Endothelial cells in culture: A model to study in vitro vascular toxicity.
AU Chappey, O.; Wautier, M.-P.; Wautier, J.-L. (1)
CS (1) Lab. Biol. Vasculaire, Hop. Lariboisere, 2 rue Ambroise Pare, 75010 Paris France
SO Toxicology In Vitro, (1995) Vol. 9, No. 4, pp. 411-419.
ISSN: 0887-2333.
DT Article
LA English
AB This review discusses the importance of cultured endothelial cells in the evaluation of the potential toxicity of a drug and for understanding the toxic effects of some compounds on the vascular system. Vascular toxicity is observed when subjects are exposed to chemicals present in the air or after ingestion of xenobiotics or drugs. Furthermore, some drugs can lead to side-effects owing to an alteration of endothelial cell function.

Endothelial cells of human and animal origin can be cultured and several of their properties can be studied using different experimental systems. Cyclosporin and penicillamine have been shown to reduce **angiogenesis** in vitro, as has also been reported for monocrotaline pyrrole. Other components, such as pyrrolizidine alkaloid, were found to be cytotoxic, as demonstrated by chromium-51 or lactate dehydrogenase release. More subtle changes can be detected in peroxidation, phospholipase activity and prostacyclin production. Endothelial cells cultured to confluency can be used to measure in vitro permeability to radiolabelled inulin or albumin. **Tunicamycin**, an inhibitor of glycosylation, increases permeability. Xenobiotics such as lead inhibit the production of plasminogen activator (t-PA) or by disrupting the thromboxane-A-2/prostacyclin balance, which promotes a thrombotic process.

CC Cytology and Cytochemistry - Human *02508
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Enzymes - Physiological Studies *10808
Cardiovascular System - Physiology and Biochemistry *14504
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Endocrine System - General *17002
Pharmacology - General *22002
Toxicology - Pharmacological Toxicology *22504
Tissue Culture, Apparatus, Methods and Media 32500
In Vitro Studies, Cellular and Subcellular *32600

BC Hominidae *86215

IT Major Concepts
Cardiovascular Medicine (Human Medicine, Medical Sciences); Cardiovascular System (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Pharmacology; Toxicology

IT Chemicals & Biochemicals
CYCLOSPORINE; PENICILLAMINE; **TUNICAMYCIN**; THROMBOXANE A-2; PROSTACYCLIN; LACTATE DEHYDROGENASE

IT Miscellaneous Descriptors
CYCLOSPORINE; LACTATE DEHYDROGENASE; PENICILLAMINE; PLASMINOGEN ACTIVATOR; PROSTACYCLIN; THROMBOSIS; THROMBOXANE A-2; **TUNICAMYCIN**

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN 59865-13-3Q (CYCLOSPORINE)
63798-73-2Q (CYCLOSPORINE)
52-67-5 (PENICILLAMINE)
11089-65-9 (TUNICAMYCIN)
57576-52-0 (THROMBOXANE A-2)
35121-78-9 (PROSTACYCLIN)
9001-60-9 (LACTATE DEHYDROGENASE)

L177 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1991:46316 BIOSIS
DN BA91:24597
TI CHARACTERIZATION OF THE RECEPTORS FOR VASCULAR ENDOTHELIAL GROWTH FACTOR.
AU VAISMAN N; GOSPODAROWICZ D; NEUFELD G
CS DEP. OF BIOL., TECHNION, ISRAEL INST. OF TECHNOL., TECHNION CITY, HAIFA 32000, ISRAEL.
SO J BIOL CHEM, (1990) 265 (32), 19461-19466.

CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB Vascular endothelial growth factor (vEGF) is a recently discovered mitogen for endothelial cells. It is also a potent **angiogenic** factor. We have characterized the vEGF receptors of endothelial cells using both binding and cross-linking techniques. Scatchard analysis of equilibrium binding experiments revealed two types of high-affinity binding sites on the cell surfaces of bovine endothelial cells. One of the sites has a dissociation constant of 10-12 M and is present at a density of 3 .times. 103 receptors/cell. The other has a dissociation constant of 10-11 M, with 4 .times. 104 receptors/cell. A high molecular weight complex containing 125I- vEGF is formed when 125I-vEGF is cross-linked to bovine endothelial cells. This complex has an apparent molecular mass of 225 kDa. Two other faintly labeled complexes with apparent molecular masses of 170 and 195 kDa also are detected. Reduction in the presence of dithiothreitol causes a substantial increase in the labeling intensity of the 170- and 195-kDa complexes, suggesting that these complexes are derived from the 225-kDa complex by reduction of disulfide bonds. The labeling of the vEGF receptors was inhibited by an excess of unlabeled vEGF but not by high concentrations of several other growth factors. Suramin and protamine, as well as several species of lectins, inhibited the binding. The expression of functional vEGF receptors was inhibited when the cells were preincubated with **tunicamycin**, indicating that glycosylation of the receptor is important for the expression of functional vEGF receptors. Pretreatment with swainsonine on the other hand, did not prevent formation of functional receptors. However, the mass of the 225-kDa complex is decreased by 20 kDa when 125I-vEGF is cross-linked to swainsonine-treated endothelial cells.
CC Cytology and Cytochemistry - Animal *02506
Biochemical Methods - Proteins, Peptides and Amino Acids 10054
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Cardiovascular System - Physiology and Biochemistry *14504